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Med. Dept.

TRANSACTIONS

OF THE

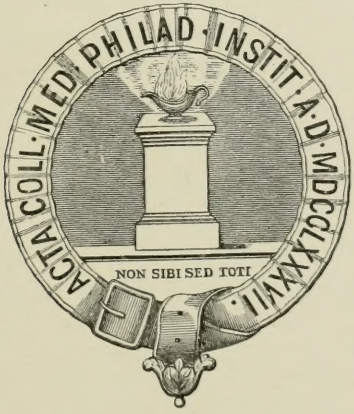
COLLEGE OF PHYSICIANS

OF

PHILADELPHIA

THIRD SERIES

VOLUME THE THIRTY-SEVENTH



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PHILADELPHIA
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1915

NOTICE.

The present volume of TRANSACTIONS contains the papers read before the College from January, 1915, to December, 1915, inclusive.

The Committee of Publication thinks it proper to say that the College holds itself in no way responsible for the statements, reasonings, or opinions set forth in the various papers published in its TRANSACTIONS.

EDITED BY

WALTER G. ELMER, M.D.

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"This volume is published in part by the income from the Francis Houston Wyeth Fund."

DORNAN, PRINTER

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1805	WILLIAM SHIPPEN
1809	ADAM KUHN
1818	THOMAS PARKE
1835	THOMAS C. JAMES[1]
1835	THOMAS T. HEWSON
1848	GEORGE B. WOOD
1879	W. S. W. RUSCHENBERGER
1883	ALFRED STILLÉ
1884	SAMUEL LEWIS[2]
1884	J. M. DA COSTA
1886	S. WEIR MITCHELL
1889	D. HAYES AGNEW
1892	S. WEIR MITCHELL
1895	J. M. DA COSTA
1898	JOHN ASHHURST, JR.
1900	W. W. KEEN
1902	HORATIO C. WOOD
1904	ARTHUR V. MEIGS
1907	JAMES TYSON
1910	GEORGE E. DE SCHWEINITZ
1913	JAMES CORNELIUS WILSON

[1] Died four months after his election.
[2] Resigned on account of ill-health.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

1915

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FELLOWS

OF THE

COLLEGE OF PHYSICIANS OF PHILADELPHIA

DECEMBER, 1915

* Non-resident Fellows.
† Fellows who have commuted dues.

ELECTED

1892. Abbott, Alexander C., M.D., Sc.D. (Hon.), Professor of Hygiene and Bacteriology in the University of Pennsylvania; Member of the Board of Health of Philadelphia. 4229 Baltimore Ave.

1912. Addison, William H. F., A.B., M.B., Assistant Professor of Normal Histology and Embryology in the University of Pennsylvania. Medical Laboratories, University of Pennsylvania.

1905. Adler, Lewis H., Jr., M.D., Professor of Diseases of the Rectum in the Philadelphia Polyclinic and College for Graduates in Medicine; formerly Prosector to the Professor of Anatomy in the University of Pennsylvania; Consulting Surgeon to the Charity Hospital. 1610 Arch St.

1914. Aiken, Thomas Gerald, M.D., Assistant Visiting Physician to the Chester County Hospital, West Chester, Pa.; Pathologist to the Country Branch of the Rush Hospital for Tuberculosis. Berwyn, Pa.

1913. Alexander, Emory G., M.D., Surgeon to St. Christopher's Hospital for Children; Associate Surgeon to the Episcopal Hospital; Clinical Professor of Surgery in the Woman's Medical College of Pennsylvania, and Demonstrator of Fracture Dressings in the Jefferson Medical College; Assistant Surgeon to the Kensington Hospital for Women. 1627 Oxford St.

ELECTED

1903. Allen, Alfred Reginald, M.D., Lecturer on Neurological Electrotherapeutics and Instructor in Neurology and Neuropathology in the University of Pennsylvania. 2013 Spruce St.

1906. Allen, Francis Olcott, Jr., A.B., M.D., Assistant Surgeon to the Presbyterian, Pennsylvania, Children's and Bryn Mawr Hospitals. 2216 Walnut St.

1896. Allyn, Herman B., M.D., Associate in Medicine in the University of Pennsylvania; Physician to the Philadelphia General Hospital. 501 S. Forty-second St.

1888. Anders, James M., M.D., L.L.D., Professor of Medicine and Clinical Medicine in the Medico-Chirurgical College; Officer de l'Instruction Publique. 1605 Walnut St.

1905. Anspach, Brooke M., M.D., Associate in Gynecology in the University of Pennsylvania; Surgeon to the Gynecean Hospital; Gynecologist to the Philadelphia General and the Stetson Hospitals; Assistant Gynecologist to the University Hospital. 119 S. Twentieth St.

1905. Appleman, Leighton F., M.D., Demonstrator of Pharmacy and Materia Medica, and Instructor in Therapeutics in the Jefferson Medical College; Instructor in Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmologist to the Frederick Douglass Memorial Hospital. 308 S. Sixteenth St.

1906. Ashhurst, Astley Paston Cooper, A.B., M.D., Instructor in Surgery in the University of Pennsylvania; Surgeon to the Episcopal Hospital and to the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases. 811 Spruce Street.

1893. Ashton, Thomas G., M.D., Physician to the Philadelphia General Hospital. 1814 S. Rittenhouse Square.

1914. Austin, J. Harold, B.S. (Univ. of Penna.), M.D., Department of Research Med., University of Pennsylvania.

1906. Babbitt, James A., A.B., (Yale), A.M. (Haverford), M.D., Professor of Hygiene and Physical Education at Haverford College; Assistant Laryngologist and Aurist, and Chief of the Out-patient Department for Diseases of the Nose, Throat, and Ear at the German Hospital; Assistant Instructor in Otology in the University of Pennsylvania; Laryngologist to the Out-patient Department of the Children's Hospital. 1901 Chestnut St.

ELECTED

1910. Baer, Benjamin F., Jr., M.D. 2040 Chestnut St.

†1892. Baker, George Fales, B.S., M.D. 1818 Spruce St.

1911. Baldwin, James Harvey, A.B., M.D., Assistant Surgeon to the Methodist Hospital. 1426 Pine St.

1889. Baldy, John Montgomery, M.D., Professor of Gynecology in the Philadelphia Polyclinic; Surgeon to the Gynecean Hospital; Consulting Surgeon to the Jewish and the Frederick Douglass Memorial Hospitals. 2219 De Lancey Place.

1898. Balliet, Tilghman M., A.M., M.D., Professor of Therapeutics at Dartmouth College, Hanover, N. H.; Physician to the Old Man's Home. 3709 Powelton Ave.

1911. Barnard, Everett P., M.D., Obstetrician to the Maternity Hospital; Assistant Instructor in Obstetrics in the University of Pennsylvania. 119 S. Nineteenth St.

1883. Baum, Charles, A.M., M.D., Ph.D. 1828 Wallace St.

1908. Beardsley, Edward J. G., M.D., L.R.C.P. (Lond.), Associate Professor of Clinical Medicine in the Jefferson Medical College; Chief Clinical Assistant in the Out-patient Medical Department of the Jefferson Medical College Hospital; Assistant Physician to the Jefferson and Philadelphia Hospitals. 2030 Chestnut St.

*1874. Bennett, W. H., A.M., M.D., Physician-in-Charge of the Seashore House for Invalid Children, and of the Seaside House for Invalid Women, Atlantic City; formerly Physician to the Episcopal Hospital, and Physician-in-Charge of St. Christopher's Hospital for Children. Children's Seashore Home, Atlantic City, N. J.

1896. Beyea, Henry D., M.D., Associate in Gynecology and Assistant Demonstrator of Obstetrics in the University of Pennsylvania; Assistant Surgeon to the Gynecean Hospital. 1734 Spruce St.

†1884. Biddle, Alexander W., M.D. Chestnut Hill.

*1903. Biggs, Montgomery H., M.D., Surgeon to the Rutherford Hospital; Chief Surgeon of the Carolina, Churchfield and Ohio Railway. Rutherfordton, N. C.

1908. Bland, Pascal Brooke, M.D., Chief Clinical Assistant in the Gynecological Department of the Jefferson Medical College Hospital; Instructor in Gynecology in the Jefferson Medical College; Gynecologist to St. Joseph's Hospital; Assistant Gynecologist to the Philadelphia General Hospital. 1621 Spruce St.

ELECTED

1894. Bochroch, Max H., M.D., Demonstrator of Neurology and Chief Clinical Assistant in the Nervous Department of the Jefferson Medical College Hospital; Neurologist to the Out-patient Department of St. Joseph's Hospital. 1539 Pine St.

1896. Boger, John A., A.M., M.D., Surgeon to St. Mary's Hospital; Surgeon to the Stetson Hospital; Surgeon to the Dispensary of the Episcopal Hospital. 2213 N. Broad St.

1910. Boice, J. Morton, A.B., M.D., Gynecologist to the Out-patient Department of St. Joseph's Hospital; Lecturer on Chemistry to the Training School of St. Joseph's Hospital; Obstetric Registrar to the Philadelphia General Hospital. 4020 Spruce St.

1911. Bonney, Charles W., A.B., M.D., Demonstrator of Applied Anatomy in the Jefferson Medical College; Assistant Surgeon, Department of Oral Surgery, Philadelphia General Hospital. 1117 Spruce St.

1913. Boston, L. Napoleon, A.M., M.D., Professor of Physical Diagnosis in the Medico-Chirurgical College; Physician to the Philadelphia General Hospital; Pathologist to the Frankford Hospital. 1819 Chestnut St.

1891. Boyd, George M., M.D., Professor of Obstetrics in the Medico-Chirurgical College; Obstetrician to the Medico-Chirurgical Hospital; Physician to the Philadelphia Lying-in Charity; Obstetrician and Gynecologist to the Philadelphia General Hospital. 1909 Spruce St.

1907. Boyer, Henry Percival, M.D., Physician to the Stetson Hospital; Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Chief Medical Inspector Pennsylvania Department of Health. 4602 Baltimore Ave.

1907. Bradley, William N., Ph.G., M.D., Visiting Pediatrist to Howard Hospital; Visiting Physician to the Out-patient Department of the Children's Hospital; Visiting Physician to the Southern Home for Destitute Children. 1638 S. Broad St.

1903. Branson, Thomas F., M.D., Attending Physician to the Bryn Mawr Hospital. Rosemont, Pa.

1891. Brinton, Lewis, M.D., Physician-in-Chief to the American Hospital for Diseases of the Stomach. 1933 Spruce St.

1900. Brinton, Ward, A.M., M.D., Visiting Physician to the Tuberculosis Department of the Philadelphia General

ELECTED

Hospital; Visiting Physician to the Hospital for Poor Consumptives at White Haven, Pa.; Visiting Physician to the Philadelphia Jewish Sanatorium for Consumptives. 1423 Spruce St.

1907. Brooks, Macy, A.B. (Princeton), M.D., Assistant Genito-urinary Surgeon to the Philadelphia General Hospital. 1314 Spruce St.

1887. Brubaker, Albert P., A.M., M.D., Professor of Physiology and Medical Jurisprudence in the Jefferson Medical College; Professor of Physiology and Hygiene in the Drexel Institute of Science, Art, and Industry. 105 N. Thirty-fourth St.

1906. Burns, Stillwell C., M.D., Lecturer on Surgery in the Medico-Chirurgical College; Assistant Surgeon to the Medico-Chirurgical Hospital. 1326 Spring Garden St.

1892. Burr, Charles W., M.D., Professor of Mental Diseases in the University of Pennsylvania; Neurologist to the Philadelphia General Hospital. 1918 Spruce St.

1906. Butler, Ralph, M.D., Professor of Diseases of the Nose and Throat in the Philadelphia Polyclinic and the College for Graduates in Medicine; Chief of the Dispensary for Diseases of the Ear at the University Hospital; Instructor in Otology in the University of Pennsylvania; Laryngologist and Aurist to the German Hospital. 1926 Chestnut St.

1912. Butt, William Redfield, M.D., Assistant Laryngologist to the Out-patient Department of the German Hospital; Chief of the Out-Patient Department for Diseases of the Ear, Nose, and Throat of the Howard Hospital; Demonstrator of Operative Rhinology in the Philadelphia Polyclinic. 1701 Chestnut St.

*1908. Cadbury, William W., A.M., M.D., University Medical School, Canton, China.

†1907. Cadwalader, Williams B., M.D., Pathologist and Clinical Assistant to the Orthopædic Hospital and Infirmary for Nervous Diseases; Assistant Instructor in Nervous Diseases in the Philadelphia Polyclinic. 1710 Locust St.

1905. Cameron, George A., M.D., Physician to the Germantown Hospital. S. E. cor. Schoolhouse Lane and Greene St., Germantown.

1905. Carmany, Harry S., M.D., Surgeon to St. Timothy's Hospital, Roxborough; Surgeon to the Dispensary of the Episcopal Hospital. 366 Green Lane, Roxborough.

ELECTED

1910. Carnett, John Berton, M.D., Associate in Surgery in the University of Pennsylvania; Assistant Surgeon to the University and the Philadelphia General Hospitals; Surgeon to the Chestnut Hill Hospital; Consulting Surgeon to the Henry Phipps Institute, to the Phœnixville Hospital, and to the Eastern Pennsylvania Institution for the Feeble-minded and Epileptic. 123 S. Twentieth St.

1905. Carpenter, Herbert B., M.D., Physician to the Dispensary of the Children's Hospital. 1805 Spruce St.

1895. Carpenter, John T., M.D., Lecturer on Ophthalmology in the University of Pennsylvania; Assistant Ophthalmic Surgeon to the University Hospital; Attending Ophthalmologist to the Bryn Mawr Hospital. 2040 Chestnut St.

1892. Cattell, Henry W., A.M., M.D., Editor of *International Clinics*, of *Medical Notes and Queries*. 3709 Spruce St.

1900. Chance, Burton, M.D., Assistant Surgeon to the Wills Eye Hospital; Ophthalmic Surgeon to the Pennsylvania Railroad Company. 235 S. Thirteenth St.

*1868. Cheston, D. Murray, M.D. Harwood P. O., Md.

1897. Cheston, Radcliffe, M.D., Visiting Physician to the Chestnut Hill Hospital; Consulting Physician to the Germantown Hospital, and to the Pennsylvania Institution for the Deaf and Dumb. Chestnut Hill.

1904. Christian, Hilary M., M.D., Clinical Professor of Genito-urinary Diseases in the Medico-Chirurgical College. 1321 Spruce St.

1903. Chrystie, Walter, M.D. Bryn Mawr, Pa.

1899. Clark, John G., M.D., Professor of Gynecology in the University of Pennsylvania; Gynecologist-in-Chief to the University Hospital. 2017 Walnut St.

1897. Claxton, Charles, A.M., M.D. 5137 Morris St., Germantown.

1896. Cleveland, Arthur H., M.D., Clinical Professor of Laryngology in the Medico-Chirurgical College; Laryngologist to the Medico-Chirurgical Hospital; Laryngologist and Aurist to the Presbyterian Hospital, and to Pennsylvania Institution for Deaf and Dumb. 256 S. Fifteenth St.

1910. Cloud, J. Howard, M.D., Assistant Physician to the Bryn Mawr Hospital; Attending Physician to the Children's House of Bryn Mawr Hospital. 7 W. Lancaster Ave., Ardmore, Pa.

1903. Coates, George Morrison, A.B., M.D., Surgeon to the Out-Patient Department for Diseases of the Ear, Throat, and Nose of the Pennsylvania Hospital; Professor of Dis-

ELECTED

eases of the Ear in the Philadelphia Polyclinic; Laryngologist to the Tuberculosis Department of the Philadelphia General Hospital; Consulting Laryngologist to the Philadelphia Orphanage. 1736 Pine St.

1908. Codman, Charles A. E., M.D., Physician to the American Oncologic Hospital. 4116 Spruce St.

1907. Cohen, Myer Solis, A.B., M.D., Pediatrist to the Jewish Hospital, and to the Philadelphia Jewish Sanatorium for Consumptives, Eagleville, Pa.; Assistant Visiting Physician to the Philadelphia General Hospital; Consulting Physician to the Home for Consumptives, Chestnut Hill. 4102 Girard Ave.

1888. Cohen, Solomon Solis, M.D., Professor of Clinical Medicine in the Jefferson Medical College; Physician to the Jefferson Medical College Hospital, to the Philadelphia General Hospital, to the Jewish Hospital, and to the Rush Hospital. 1525 Walnut St.

1898. Coles, Stricker, M.D., Assistant Professor of Obstetrics in the Jefferson Medical College; Assistant Obstetrician to the Jefferson and the Philadelphia General Hospitals; Visiting Physician to the Philadelphia Lying-in-Charity Hospital. 2103 Walnut St.

1901. Coley, Thomas Luther, A.B., M.D., Attending Physician Methodist Episcopal Hospital, Philadelphia. 256 S. Fifteenth St.

1903. Coplin, W. M. L., M.D., Professor of Pathology in the Jefferson Medical College; Pathologist to and Director of the Laboratories of the Jefferson Medical College Hospital; Pathologist to the Philadelphia General Hospital and to the Friends' Asylum for the Insane, Frankford; Bacteriologist to the Pennsylvania State Board of Health. 606 S. Forty-eighth St.

1912. Copp, Owen, A.B., M.D., Physician-in-chief and Superintendent of the Pennsylvania Hospital for the Insane. Pennsylvania Hospital for the Insane, Forty-fourth and Market Streets.

1911. Cornell, Walter Stewart, A.B., M.D., Director of Medical Inspection of Public Schools of the City of Philadelphia; Chief of Medical Staff of the House of Detention; Lecturer on Osteology in the University of Pennsylvania; Lieutenant, Medical Reserve Corps, U. S. A. 729 City Hall.

ELECTED

1914. Corson, Edward Foulke, M.D., Physician for Diseases of the Skin, Presbyterian Hospital Dispensary; Assistant Dermatologist, Children's Hospital Dispensary. Cynwyd, Pa.

1907. Council, Malcolm S., M.D., Attending Physician to the Bryn Mawr Hospital; Attending Physician to the Cathcart Home at Devon. Bryn Mawr, Pa.

*1909. Craig, Alexander R., A.M., M.D. 535 N. Dearborn St., Chicago, Ill.

1904. Craig, Frank A., M.D., Instructor in Medicine in the University of Pennsylvania; Visiting Physician to the Henry Phipps Institute, University of Pennsylvania; Visiting Physician to the White Haven Sanatorium; Physcian-in-Charge of the Tuberculosis Class of the Presbyterian Hospital. 2030 Chestnut St.

1907. Crampton, George S., M.D., Attending Surgeon to the Eye Department of the Pennsylvania Hospital and the Philadelphia Hospital for Contagious Diseases; Assistant Surgeon to the Wills Hospital; Lecturer on Physiologic Optics in the Philadelphia Polyclinic and School for Graduates in Medicine; Ophthalmologist to the Philadelphia Orphanage. 1700 Walnut St.

1904. Cruice, John M., M.D., Physician to the Henry Phipps Institute of the University of Pennsylvania; Physician to the Medical Dispensary of St. Agnes' Hospital; Instructor in Medicine in the University of Pennsylvania. 1820 Pine St.

*1910. Cummins, W. Taylor, M.D., Pathologist to the Southern Pacific Hospital; Director of the Mary W. Harriman Research Laboratory, San Francisco, Cal.

1902. Currie, Charles A., M.D., Physician to the Germantown Hospital. West Walnut Lane, Germantown.

1903. Da Costa, John C., Jr., M.D., Associate Professor of Medicine in the Jefferson Medical College; Assistant Physician to the Jefferson Medical College Hospital; Hematologist to the German Hospital; Consulting Physician to the Northwestern General Hospital. 264 S. Fifteenth St.

1896. Da Costa, John Chalmers, M.D., Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General and St. Joseph's Hospitals. 2045 Walnut St.

1887. Daland, Judson, M.D., Professor of Clinical Medicine in the Medico-Chirurgical College; Physician to the Medico-Chirurgical Hospital. 317 S. Eighteenth St.

ELECTED

1859. Darrach, James, M.D., Consulting Surgeon to the Germantown Hospital. 5923 Greene St., Germantown.

1896. Davis, Charles N., M.D., Dermatologist to the Pennsylvania Hospital; Consulting Dermatologist to St. Agnes' Hospital; Assistant Physician to the Dispensary for Skin Diseases in the Howard Hospital. 1931 Spruce St.

1888. Davis, Edward P., A.M., M.D., Professor of Obstetrics in the Jefferson Medical College and in the Philadelphia Polyclinic; Visiting Obstetrician to the Jefferson and the Polyclinic Hospitals; Obstetrician and Gynecologist to the Philadelphia General Hospital. 250 S. Twenty-first St.

1889. Davis, Gwilym G., M.D. (Univ. of Penna. and Göttingen), LL.D., M.R.C.S. (Eng.), Professor of Orthopedic Surgery in the University of Pennsylvania; Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases; Orthopedic Surgeon to the Philadelphia General Hospital; Consulting Surgeon to St. Joseph's Hospital. 1814 Spruce St.

1900. Davisson, Alex. Heron, M.D. 31 St. Paul's Rd., Ardmore.

1894. Deaver, Harry C., M.D., Professor of Surgery in the Woman's Medical College of Pennsylvania; Surgeon to the Episcopal Hospital, and to the Children's Hospital of the Mary J. Drexel Home; Surgeon-in-Chief to the Kensington Hospital for Women. 1534 N. Fifteenth St.

1887. Deaver, John B., M.D., D.Sc., LL.D., Professor of the Practice of Surgery in the University of Pennsylvania; Surgeon-in-Chief to the German Hospital. 1634 Walnut St.

1902. Dehoney, Howard, M.D. 237 S. Thirteenth St.

1885. Dercum, Francis X., A.M., M.D., Ph.D., Professor of Nervous and Mental Diseases in the Jefferson Medical College; Consulting Neurologist to the Philadelphia General Hospital; Foreign Corresponding Member of the Neurological Society of Paris, and Corresponding Member of the Psychiatric and Neurological Society of Vienna. 1719 Walnut St.

1908. Despard, Duncan L., M.D., Surgeon to the Abington Memorial Hospital; Assistant Surgeon to the Jefferson Medical College Hospital; Demonstrator of Clinical Surgery in the Jefferson Medical College; Associate in Gynæcology in the Philadelphia Polyclinic Hospital. 1806 Pine St.

1912. Dewey, J. Hiland, Ph.B., M.D., Assistant Surgeon to Wills Eye Hospital; Ophthalmic Surgeon to St. Francis' Hospital, Trenton, N. J. 1436 Diamond St.

ELECTED

1911. Dickson, Frank D., M.D., Instructor in Orthopedic Surgery in the University of Pennsylvania; Assistant Orthopedic Surgeon to the University Hospital; Assistant Surgeon to the Orthopædic Hospital; Assistant Orthopedic Surgeon to the Philadelphia General Hospital. 1814 Spruce Street.

1908. Dillard, Henry K., Jr., M.D., Physician to the Out-patient Department of the Pennsylvania Hospital; Physician to the Dispensary of the Mary J. Drexel Home. 234 S. Twentieth St.

1891. Dixon, Samuel G., M.D., LL.D., Commissioner of Health of Pennsylvania; President of the Academy of Natural Sciences of Philadelphia; Member of the Philadelphia Bar. Bryn Mawr, Pa.

*1897. Dorland, W. A. Newman, A.M., M.D., Professor of Gynecology in the Post-graduate Medical School of Chicago; Professor of Obstetrics in the Chicago College of Medicine and Surgery; Visiting Obstetrician to Cook County Hospital; First Lieutenant, Medical Reserve Corps, U. S. Army. 7 West Madison St., Chicago, Ill.

1907. Dorrance, George Morris, M.D., Surgeon to St. Agnes' Hospital; Demonstrator of Applied Anatomy in the Dental Department of the University of Pennsylvania. 2025 Walnut St.

1893. Downs, Norton, M.D., Fordhooke Farms, Three Tuns, Pa.

1864. Downs, R. N., M.D., Consulting Physician to the Germantown Hospital. 5916 Greene St., Germantown.

1902. Downs, Robert N., Jr., M.D., Surgeon to the Dispensary of the Germantown Hospital. 6008 Greene St., Germantown.

1910. Drayton, William, Jr., M.D., Physician to the Philadelphia Hospital for Contagious Diseases; Physician to the Out-patient Department of the Pennsylvania Hospital; Physician to the Pennsylvania Institute for the Instruction of the Blind; Assistant Physician to the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases. 1316 Locust Street.

*1864. Duer, Edward L., A.M., M.D. Odessa, Delaware.

1881. Dulles, Charles Winslow, M.D., Consulting Surgeon of the Rush Hospital. 4101 Walnut St.

ELECTED

1911. Earnshaw, Henry Culp, M.S., M.D., Attending Physician to the Hospital of the Good Shepherd, Rosemont; Assistant Attending Physician to the Bryn Mawr Hospital; Attending Physician to the Bryn Mawr Children's Hospital; Pennsylvania Railroad Surgeon. Bryn Mawr, Pa.

*1887. Edwards, William A., M.D., Professor of Pediatrics in the Medical Department of the University of California. Fifth and Spring Sts., Los Angeles, Cal.

1911. Eliason, Eldridge E., B.A., M.D., Assistant Instructor in Surgery in the University of Pennsylvania; Assistant Surgeon to the University Hospital; Assistant Surgeon to the Howard Hospital; Surgeon to the Out-patient Department of the Children's Hospital. 320 S. Sixteenth Street.

1904. Elmer, Walter G., B.S., M.D., Instructor in Orthopedic Surgery in the University of Pennsylvania; Assistant Orthopedic Surgeon to the University Hospital; Orthopedic Surgeon to the Jewish Hospital; Surgeon to the Pennsylvania Training School for Children. 1801 Pine Street.

1896. Ely, Thomas C., A.M., M.D. 2041 Green St.

1901. Erck, Theodore A., M.D., Associate in Gynecology in the Philadelphia Polyclinic and College for Graduates in Medicine; Associate Surgeon to the Gynecean Hospital. 251 S. Thirteenth St.

1893. Eshner, Augustus A., M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine; Physician to the Philadelphia General Hospital; Assistant Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Consulting Physician to Mercy Hospital. 1019 Spruce St.

*1905. Evans, Joseph S., Jr., A.B., M.D., Professor of Clinical Medicine in the University of Wisconsin; Consulting Physician, Madison General Hospital. University of Wisconsin, Madison, Wis.

1905. Evans, William, M.D. 4007 Chestnut St.

1912. Eves, Curtis C., M.D., Aural and Laryngeal Surgeon to the Episcopal Hospital; Assistant in the Out-patient Department for Diseases of the Ear, Throat, and Nose of the Pennsylvania Hospital; Demonstrator of Operative Surgery of the Ear, Nose, and Throat in the Philadelphia Polyclinic. 302 S. Nineteenth St.

ELECTED

1894. Faries, Randolph, M.D. 2007 Walnut St.

†1903. Farr, Clifford B., A.B., M.D., Professor of Diseases of the Stomach, etc., in the Philadelphia Polyclinic; Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Philadelphia General Hospital; Pathologist to the Presbyterian Hospital. 117 S. Twenty-second Street.

1893. Farr, William W., M.D., Physician to the Leamy Home. Springfield Ave. and Lincoln Drive, Chestnut Hill.

1884. Fenton, Thomas H., M.D., Ophthalmologist to St. Vincent's Home, to the Home for Aged Couples, to the Baptist Home, and to the House of the Good Shepherd. 1319 Spruce St.

1907. Ferguson, Albert D., M.D., Physician-in-charge of the Widener Memorial School for Crippled Children. 50 E. Johnson St., Germantown.

1907. Fetterolf, George, A.B., M.D., Sc.D., Laryngologist to the Henry Phipps Institute for Tuberculosis; Laryngologist to the White Haven Sanatorium; Consulting Laryngologist to the Phœnixville Hospital; Demonstrator of Anatomy in the University of Pennsylvania. 330 S. Sixteenth St.

1907. Fife, Charles A., A.B., M.D., Instructor in Pediatrics in the University of Pennsylvania; Pediatrist to the Presbyterian Hospital; Physician to the St. Christopher's Hospital for Children; Assistant Physician to the Philadelphia General Hospital. 2033 Locust St.

1884. Fisher, Henry M., M.D. 1027 Pine St.

1910. Fisher, John Monroe, M.D., Associate Professor of Gynecology in the Jefferson Medical College; Gynecologist to the Philadelphia, St. Agnes', and Phœnixville Hospitals; Assistant Gynecologist to the Jefferson Medical College Hospital. 222 S. Fifteenth St.

1888. Flick, Lawrence F., M.D. 736 Pine St.

1908. Foulkrod, Collin, M.D., Obstetrician to the Maternity House of the Presbyterian Hospital; Assistant Demonstrator of Obstetrics in Jefferson Medical College; Gynecologist to the Dispensary of the Presbyterian Hospital. 4005 Chestnut St.

1908. Fox, Herbert, M.D., Director of the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania; Pathologist to the Laboratory of Comparative Pathology

ELECTED

of the Zoölogical Society of Philadelphia; Pathologist to the Rush Hospital; Pathologist to the Children's Hospital. 3902 Locust St.

†1885. Fox, Joseph M., M.D. Torresdale, Pa.

1906. Fraley, Frederick, Jr., A.B., M.D. 1701 De Lancey Place.

1903. Francine, Albert Philip, A.M., M.D., Associate in Medicine in the University of Pennsylvania; Visiting Physician to the Philadelphia General Hospital, Department of Tuberculosis; Physician-in-Chief to the State Dispensary for Tuberculosis, Philadelphia. 1932 Spruce St.

1897. Frazier, Charles H., A.B., M.D., Sc.D., Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University Hospital. 1724 Spruce St.

†1890. Freeman, Walter J., M.D., Emeritus Professor of Laryngology in the Philadelphia Polyclinic; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb. 1832 Spruce St.

*1910. Frescoln, Leonard D., A.B., M.D., United States Physician Indian Service; First Lieutenant, Army Medical Reserve. Army Medical School. Washington, D. C.

1910. Furbush, Charles Lincoln, M.D. 1501 Spruce St.

1889. Fussell, M. Howard, M.D., Professor of Applied Therapeutics in the University of Pennsylvania; Physician to the University Hospital, the Episcopal Hospital, St. Timothy's Hospital, and St. Mary's Hospital. 2035 Walnut St.; 421 Lyceum Ave., Roxborough.

1899. Gamble, Robert G., M.D., one of the Attending Physicians to the Bryn Mawr Hospital. Haverford, Pa.

1912. Gaskill, Henry Kennedy, M.D., Assistant Professor of Dermatology in the Jefferson Medical College; Attending Dermatologist to the Philadelphia General Hospital. 1610 Spruce St.

1873. Gerhard, George S., M.D., Physician-in-Chief to the Bryn Mawr Hospital; Consulting Physician to Bryn Mawr College; Consulting Physician to Villa Nova College. Fifty-eighth Street and Overbrook Ave.

1902. Ghriskey, Albert A., M.D. 3936 Walnut St.

1899. Gibbon, John H., M.D., Professor of Surgery in the Jefferson Medical College; Surgeon to the Pennsylvania and the Bryn Mawr Hospitals. 1608 Spruce St.

ELECTED

1908. Gildersleeve, Nathaniel, M.D., Professor of Microbiology and Bacteriopathology; The Thomas W. Evans Museum and Dental Institute School of Dentistry University of Pennsylvania. School of Dentistry, University of Pennsylvania.

1913. Ginsburg, Nathaniel, M.D., Surgeon to the Jewish Hospital; Associate in Surgery in the Philadelphia Polyclinic and College for graduates in Medicine; Assistant Surgeon to Mt. Sinai Hospital; Instructor in Anatomy in the University of Pennsylvania. 1704 Pine St.

1897. Girvin, John H., M.D., Physician for Diseases of Women at the Presbyterian Hospital; Instructor in Obstetrics in the University of Pennsylvania. 2120 Walnut St.

1906. Gittings, J. Claxton, M.D., Instructor in Pediatrics in the University of Pennsylvania; Assistant Pediatric Physician to the University Hospital; Visiting Physician to the Children's Hospital of the Mary J. Drexel Home, and to the Out-patient Department of the Presbyterian Hospital. 3903 Chestnut St.

1905. Given, Ellis E. W., M.D., Surgeon to the Dispensary of the Episcopal Hospital. 2714 Columbia Avenue.

1894. Gleason, E. B., S.B., M.D., LL.D., Professor of Otology in the Medico-Chirurgical College. 2033 Chestnut St.

1906. Goepp, R. Max, M.D., Professor of Clinical Medicine, Dean of the College Department, and Secretary of the Faculty of the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Professor of Clinical Medicine in the Jefferson Medical College; Assistant Visiting Physician to the Philadelphia General Hospital. 1716 Locust St.

1906. Goldberg, Harold G., M.D., Ophthalmic Surgeon to the Episcopal Hospital and to the Kensington Hospital for Women; First Lieutenant, Medical Reserve Corps, U. S. Army. 1925 Chestnut St.

1893. Goodell, W. Constantine, M.D. 300 S. Thirteenth St.

1908. Goodman, Edward H., M.D., Associate in Medicine in the University of Pennsylvania; Consultant to the Medical Dispensary of the University Hospital; Assistant Physician to the University Hospital; Assistant Physician to the Philadelphia General Hospital. 248 S. Twenty-first St.

1905. Gordon, Alfred, M.D., Neurologist to the Mt. Sinai, the Northwestern General, and the Douglass Memorial Hospitals. 1812 Spruce St.

ELECTED

†1897. Gould, George M., A.M., M.D. 401 Oriental Ave., Atlantic City, N. J.

1894. Graham, Edwin E., M.D., Professor of Pediatrics in the Jefferson Medical College; Pediatrist to the Jefferson and the Philadelphia General Hospitals; Physician to the Franklin Reformatory Home. 1713 Spruce St.

1885. Graham, John, M.D. 326 S. Fifteenth St.

1904. Grayson, Charles P., M.D., Professor of Laryngology and Rhinology in the University of Pennsylvania; Physician-in-Charge of the Throat and Nose Department of the University Hospital; Otolaryngologist to the Philadelphia General Hospital. 1435 Spruce St.

1910. Greenman, Milton J., M.D., Sc.D., Director of the Wistar Institute of Anatomy and Biology. Wistar Institute of Anatomy and Biology, Thirty-sixth St. and Woodland Ave.

1883. Griffith, J. P. Crozer, M.D., Professor of Pediatrics in the University of Pennsylvania; Corresponding Member of the Société de Pédiatrie de Paris. 1810 Spruce St.

1912. Griscom, J. Milton, B.S., M.D., Assistant Surgeon to the Wills Eye Hospital; Chief of Clinic of the Eye Dispensary of the Presbyterian Hospital. 1925 Chestnut St.

1911. Gummey, Frank Bird, M.D., Visiting Physician to the Germantown Hospital and Dispensary; Visiting Physician to the Midnight Mission. 5418 Greene St., Germantown.

*1902. Gwyn, Norman B., M.D., Instructor in Medicine in the University of Pennsylvania. 20 S. Twenty-first St.

1894. Hamill, Samuel McC., M.D., Professor of Diseases of Children in the Philadelphia Polyclinic and College for Graduates in Medicine; Pediatrist to the Presbyterian Hospital; Pediatrist to St. Vincent's Home. 1822 Spruce St.

1897. Hand, Alfred, Jr., M.D., Visiting Physician to the Children's Hospital, to the Children's Hospital of the Mary J. Drexel Home, and to the Methodist Hospital. 1724 Pine St.

1886. Hansell, Howard F., M.D., Professor of Ophthalmology in the Jefferson Medical College; Ophthalmic Surgeon to the Philadelphia General Hospital and to the Jefferson Medical College Hospital; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic. 1528 Walnut St.

ELECTED

1889. Hare, Hobart A., M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College, 1801 Spruce St.

1903. Hart, Charles D., M.A., M.D., Inspector of the Eastern Penitentiary; Consulting Physician to the Pennsylvania Institution for the Instruction of the Blind; Chairman of the Medical Section of the Philadelphia Vice Commission. 1317 Walnut St.

1885. Harte, Richard H., M.D., Adjunct Professor of Surgery in the University of Pennsylvania; Surgeon to the Pennsylvania and the Orthopædic Hospitals; Consulting Surgeon to St. Mary's, St. Timothy's, and the Bryn Mawr Hospitals. 1503 Spruce St.

1888. Hartzell, Milton B., M.D., LL.D., Professor of Dermatology in the University of Pennsylvania; Clinical Professor of Dermatology in the Woman's Medical College of Pennsylvania. 3644 Chestnut St.

1907. Hatfield, Charles James, A.B. (Princeton), M.D., Executive Director of the Henry Phipps Institute for the Study, Treatment, and Prevention of Tuberculosis; Visiting Physician to the White Haven Sanatorium. 2008 Walnut Street.

1872. Hays, I. Minis, M.D. 266 S. Twenty-first St.

1911. Heed, Charles R., M.D., Associate Professor of Ophthalmology in the Philadelphia Polyclinic; Instructor in Ophthalmology in the Jefferson Medical College; Ophthalmologist to Girard College. 1402 Spruce St.

1908. Heineberg, Alfred, M.D., Associate in Gynecology in the Jefferson Medical College; Assistant Gynecologist to St. Agnes' and to Mt. Sinai Hospitals. 1642 Pine St.

1901. Heisler, John C., M.D., Professor of Anatomy in the Medico-Chirurgical College. 3829 Walnut St.

1884. Henry, Frederick P., A.M., M.D., Professor of the Principles and Practice of Medicine in the Woman's Medical College of Pennsylvania; Physician to the Philadelphia General Hospital. 114 S. Eighteenth St.

1903. Henry, J. Norman, M.D., Physician to the Pennsylvania Hospital; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania; Assistant Physician to the Philadelphia General Hospital. 1906 Spruce St.

1891. Hewson, Addinell, A.B., A.M., M.D., Professor of Anatomy in the Philadelphia Polyclinic and College for Graduates in

ELECTED

Medicine; Professor of Anatomy and Histology in the Temple University; Surgeon to St. Timothy's Hospital, Roxborough. 2120 Spruce St.

1909. Higbee, William S., M.D., President of the Pennsylvania State Board of Examiners for Registration of Nurses. 1703 S. Broad St.

1910. Hill, Howard Kennedy, M.D., Assistant Instructor in Medicine in the University of Pennsylvania; Physician to the Children's Medical Dispensary of the Presbyterian Hospital; Visiting Physician to the University Settlement, and to the Day Nursery; Assistant Physician to the Medical Dispensary of the Children's Hospital. 314 S. Seventeenth Street.

1897. Hinkle, William M., M.D., Lecturer on the Anatomy and Physiology of the Vocal Organs in the National School of Elocution and Oratory. 1323 N. Thirteenth St.

*1892. Hinsdale, Guy, A.M., M.D., Associate Professor of Climatology in the Medico-Chirurgical College, Philadelphia. Hot Springs, Virginia.

1888. Hirsh, A. Bern, M.D., Physician to the Home for Aged Couples. 22 S. Twenty-first St.

1888. Hirst, Barton Cooke, A.B., M.D., LL.D., Professor of Obstetrics in the University of Pennsylvania; Gynecologist to the Philadelphia General and the Howard Hospitals. 1821 Spruce Street.

1903. Hirst, John Cooke, M.D., Assistant Obstetrician to the University and the Philadelphia General Hospitals; Attending Physician to the Maternity Hospital and to the Gynecological Dispensary of the Howard Hospital; Consulting Obstetrician to the Southeastern Dispensary. 1823 Pine St.

1908. Hitchens, Arthur Parker, M.D. Glenolden, Pa.

1905. Hodge, Edward Blanchard, A.B., M.D., Surgeon to the Presbyterian and the Children's Hospitals; Surgeon to the Out-patient Department of the Pennsylvania Hospital; Associate Surgeon to the Widener Memorial School. 346 S. Sixteenth Street.

1913. Hoffman, Clarence, M.D., 425 S. Carlisle St.

1885. Holland, James W., A.M., M.D., Sc.D., Emeritus Professor of Medical Chemistry and Toxicology and Dean of the Jefferson Medical College. 2006 Chestnut St.

ELECTED

1906. Holloway, Thomas B., M.D., Professor of Ophthalmology in the Philadelphia Polyclinic and School for Graduates in Medicine; Instructor in Ophthalmology in the University of Pennsylvania; Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases; Ophthalmologist to the Pennsylvania Institution for the Instruction of the Blind at Overbrook. 1819 Chestnut St.

1914. Hooker, Richard S., M.D. 2116 N. Hancock St.

1908. Hoyt, Daniel M., M.D., Assistant Visiting Physician to the Philadelphia General Hospital. 3604 Chestnut St.

*1912. Huber, G. Carl, M.D., Professor of Anatomy and Director of the Anatomic Laboratories in the University of Michigan. 1330 Hill St., Ann Arbor, Mich.

1892. Hughes, William E., M.D., Visiting Physician to the Philadelphia General Hospital; Pathologist to the Presbyterian Hospital. 3945 Chestnut St.

1912. Hunter, John W., B.S., M.D. 2042 Pine St.

1898. Hutchinson, James P., M.D., Surgeon to the Pennsylvania, the Methodist, the Children's, St. Timothy's, and the Bryn Mawr Hospitals; Adjunct Professor of Surgery in the University of Pennsylvania. 133 S. Twenty-second St.

1871. Ingham, James V., M.D. 1811 Walnut St.

*1885. Jackson, Edward, M.D., Professor of Ophthalmology in the University of Colorado; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic; Ophthalmologist to the Denver City and County Hospital. 318 Majestic Building, Denver, Col.

*1906. Jacobs, Francis Brinton, B.S., M.D., Assistant Surgeon to the Chester County Hospital. Whitford, Pa.

1913. Jefferys, William Hamilton, A.B., A.M., M.D., Surgeon to St. Luke's Hospital, Shanghai; Professor of Surgery in St. John's University, Shanghai; Editor of the China Medical Journal. 100 W. Walnut Lane, Germantown.

1898. Johnson, Russell H., A.B. (Princeton), M.D., Physician to the Pennsylvania Institution for the Deaf and Dumb. Chestnut Hill, Philadelphia.

1900. Jones, Charles James, A.M., M.D., LL.D., Ophthalmic Surgeon to St. Joseph's Hospital; Ophthalmic Surgeon to the House of the Good Shepherd, Germantown; Consulting Ophthalmologist to St. Vincent's Home. 1507 Locust Street.

ELECTED

1914. Jones, Isaac H., A.B., A.M., M.D. 1831 Chestnut St.

1913. Jones, John F. X., B.S., A.B., A.M., M.D., Surgeon to St. Joseph's Hospital. 1815 Spruce St.

1900. Jopson, John H., M.D., Professor of Surgery in the Philadelphia Polyclinic; Associate in Surgery in the University of Pennsylvania; Surgeon to the Presbyterian and the Children's Hospitals. 1824 Pine St.

1900. Judson, Charles F., A.B., M.D., Physician to St. Christopher's Hospital for Children, to the Southern Home for Destitute Children and to the Sheltering Arms. 1005 Spruce Street.

1902. Jump, Henry D., M.D., Instructor in Medicine in the University of Pennsylvania; Assistant Physician to the Medical Dispensary of the University Hospital. 4634 Chester Ave.

1886. Jurist, Louis, M.D. 916 N. Broad St.

1903. Kalteyer, Frederick J., M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College; Chief of the Out-patient Department, Assistant Attending Physician, and Hematologist to the Jefferson Medical College Hospital; Pathologist to Philadelphia Lying-in-Charity. 1533 Pine Street.

*1910. Karsner, Howard T., M.D., Professor of Pathology in the Western Reserve University Medical School. Lakeside Hospital, Cleveland, Ohio.

†1867. Keen, William W., M.D., LL.D., (Hon.) F.R.C.S. (Eng. and Edin.), Emeritus Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Membre Correspondant Etranger de la Société de Chirurgie de Paris; Honorary Member of the Société Belge de Chirurgie and of the Clinical Society of London; Ehren mitglied der deutschen Gesellschaft für Chirurgie. 1729 Chestnut St.

1912. Keene, Floyd E., M.D., Instructor in Gynecology in the University of Pennsylvania; Assistant Gynecologist to the University Hospital; Gynecologist to the Chestnut Hill Hospital. 116 S. Nineteenth St

1913. Kelly, Francis Joseph, M.D. 1809 Chestnut St.

*1887. Kelly, Howard A., A.B., M.D., LL.D. (Aberdeen, Wash. and Lee, and Univ. of Pa.), Professor of Gynecology in Johns Hopkins University and Gynecologist to the Johns Hopkins Hospital, Baltimore, Md.; Hon. Fellow of the

ELECTED

Edinburgh Obstetrical Society, the Royal Academy of Medicine of Ireland, and of the Glasgow Obstetrical and Gynecological Society. 1406 Eutaw Place, Baltimore, Md.

1909. Kelly, James A., A.M., M.D., Visiting Surgeon to St. Mary's and St. Timothy's Hospitals; Associate in Surgery in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Visiting Surgeon to St. Joseph's Hospital. 1510 N. Seventeenth St.

1912. Kelly, Thomas C., A.M., M.D., Assistant Instructor of Medicine in the University of Pennsylvania; Pediatrician to St. Mary's Hospital; Physician to Out-patient Department of Germantown Hospital. 105 School Lane, Germantown.

1898. Kempton, Augustus F., M.D. 2118 Pine St.

1905. Kercher, Delno E., M.D. 1534 Pine St.

1913. Klopp, Edward J., M.D., Instructor in Surgery in the Jefferson Medical College; Assistant Surgeon to the Germantown Hospital; Chief Clinical Assistant in the Surgical Department of the Jefferson Hospital; Assistant Surgeon to the Out-patient Department of the Pennsylvania Hospital. 1223 Spruce St.

1895. Kneass, Samuel S., M.D., Associate in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania. 1510 Walnut St.

1908. Knipe, Jay C., M.D., Ophthalmologist to the Jewish Hospital; Assistant Ophthalmologist to the Philadelphia General Hospital, and to the Mary J. Drexel Home; Chief of the Eye Clinic at the Jefferson Medical College Hospital; Demonstrator of Osteology and Syndesmology in the Jefferson Medical College. 2035 Chestnut St.

1908. Knowles, Frank Crozer, M.D., Instructor in Dermatology in the University of Pennsylvania; Clinical Professor of Dermatology in the Woman's Medical College; Dermatologist to the Presbyterian Hospital; Assistant Dermatologist to the Dispensary of the Pennsylvania Hospital. 2022 Spruce St.

1914. Kolmer, John A., M.D., Dr. P.H., M.Sc., Assistant Professor of Experimental Pathology in the University of Pennsylvania; Professor of Pathology and Pathologist to the Department of Dermatological Research, Philadelphia Polyclinic; Pathologist to the Philadelphia Hospital for Contagious Diseases; Serologist to St. Agnes' and St. Timothy's Hospitals. 927 S. St. Bernard St.

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1904. Krauss, Frederick, M.D., Ophthalmic Surgeon to the Episcopal Hospital; Ophthalmic and Aural Surgeon to St. Christopher's Hospital for Children and Dispensary; Ear, Nose, and Throat Physician to the Children's Seashore House for Invalid Children, Atlantic City, N. J. 1701 Chestnut St.

1905. Kremer, Walter H., M.D., 5904 Greene St., Germantown.

1914. Krumbhaar, Edward B., A.B. (Harvard), M.D., Fellow in Research Medicine and Assistant Instructor in Medicine; University of Pennsylvania; Physician to Out-patient Department, Pennsylvania Hospital. W. Mermaid La., Chestnut Hill.

1900. Krusen, Wilmer, M.D., Professor of Gynecology in the Medical Department of Temple University; Chief Gynecologist to the Samaritan and the Garretson Hospitals; Consulting Gynecologist to the Charity and Mercy Hospitals. 127 N. Twentieth St.

1897. Kyle, D. Braden, A.M., M.D., Professor of Laryngology in the Jefferson Medical College; Consulting Laryngologist, Rhinologist, and Otologist to St. Agnes' Hospital and to the Philadelphia Home for Incurables; Laryngologist to the New Jersey Training School for Feeble-minded Children; Bacteriologist to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1517 Walnut St.

1913. Laird, John Lohra, A.B., M.D., Assistant Surgeon in Genito-Urinary Diseases to the University Hospital; Associate in Serology in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania; Assistant Instructor in Genito-Urinary Surgery in the University of Pennsylvania. 247 S. Seventeenth St.

1909. Laird, J. Packard, M.D., Visiting Physician to the Devon Branch of Presbyterian Hospital of Philadelphia. Devon, Pa.

1904. Landis, Henry R. M., M.D., Director of the Clinical and Sociological Departments of the Henry Phipps Institute of the University of Pennsylvania; Assistant Professor in Medicine in the University of Pennsylvania; Visiting Physician to the White Haven Sanatorium. 11 S. Twenty-first St.

1907. Langdon, H. Maxwell, M.D., Instructor in Ophthalmology in the University of Pennsylvania; Assistant Surgeon to the Dispensary for Diseases of the Eye in the University Hospital; Assistant Ophthalmologist to the Orthopædic Hospital; Chief of the Dispensary for Diseases of the Eye of the Presbyterian Hospital. 2018 Chestnut St.

ELECTED

1887. Leaman, Henry, M.D. 832 N. Broad St.

1904. Le Boutillier, Theodore, M.D., Clinical Professor of Pediatrics in the Woman's Medical College of Pennsylvania; Pediatrist to the Woman's College Hospital; Physician to the Philadelphia Hospital for Contagious Diseases and the Babies' Hospital of Philadelphia. 9 S. Twenty-first Street.

1893. Le Conte, Robert G., A.B., M.D., Surgeon to the Pennsylvania and the Bryn Mawr Hospitals; Consulting Surgeon to Germantown and Gynecean Hospitals. 1530 Locust Street.

1908. Lee, Walter Estell, M.D., Surgeon to the Gynecological Dispensary of the Pennsylvania Hospital; Assistant Surgeon to the Germantown and Bryn Mawr Hospitals; Surgeon to the Dispensary of the Episcopal Hospital and Children's Hospital; Surgeon to the Glen Mills Schools. 905 Pine Street.

1903. Leffmann, Henry, A.M., M.D., D.D.S., Ph.D., Professor of Chemistry in the Woman's Medical College of Pennsylvania; Honorary Professor of Chemistry in the Wagner Free Institute of Science; Pathological Chemist to the Jefferson Medical College Hospital. 1839 N. Seventeenth Street.

1892. Leidy, Joseph, M.D., Officer l'instruction publique, France; Consulting Physician to the Pennsylvania Training School for Feeble-minded Children. 1319 Locust St.

1909. L'Engle, Edward M., M.D. Jacksonville, Fla.

1915. Lewis, Fielding O., M.D., Associate in Laryngology in the Jefferson Medical College Hospital; Operating Clinical Chief of the Laryngological Dispensary and Clinical Assistant of the Otological Dispensary of the Jefferson Medical College Hospital; Laryngologist of the Philadelphia General Hospital. 261 S. Seventeenth St.

1877. Lewis, Morris J., M.D., Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases and to the Pennsylvania Hospital. 1316 Locust St.

1911. Lewis, Paul A., M.D., Director of the Pathological Department of the Henry Phipps Institute of the University of Pennsylvania; Assistant Professor of Pathology in the University of Pennsylvania; Director of the Ayer Clinical Laboratory of the Pennsylvania Hospital. Henry Phipps Institute, 238 Pine St.

ELECTED

1904. Lindauer, Eugene, M.D., Instructor of Neurology in the Medico-Chirurgical Hospital; Associate in Clinical Medicine in the Philadelphia Polyclinic; Assistant Neurologist to the Philadelphia General Hospital. 2018 N. Thirty-second St.

1886. Lloyd, J. Hendrie, A.M. (Princeton), M.D., Neurologist to the Philadelphia General Hospital, and to the Methodist Episcopal Hospital; Consulting Neurologist to the State Asylum for the Chronic Insane at Wernersville, and to the Pennsylvania Training School for Feeble-minded Children at Elwyn. 116 S. Twenty-first St.

1907. Lodholz, Edward, M.D., Demonstrator of Physiology in the University of Pennsylvania. 3103 Diamond St.

1893. Longaker, Daniel, M.D., Obstetrician to the Kensington Hospital for Women and Visiting Obstetrician to the Jewish Maternity Hospital. 1402 N. Sixteenth St.

1907. Loux, Hiram R., M.D., Professor of Genito-Urinary Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General Hospital. 1819 Walnut St.

1914. Lyon, B. B. Vincent, A.B. (Williams Coll.), M.D. 1901 Pine St.

1900. McCarthy, Daniel J., M.D., Professor of Medical Jurisprudence (George B. Wood Foundation) in the University of Pennsylvania; Neurologist to the Philadelphia General and St. Agnes' Hospitals, and to the Henry Phipps Institute. 2025 Walnut St.

*1903. McConnell, Guthrie, M.D., Director of the Clinical Laboratory of the Waterloo Medical Society; Deputy State Bacteriologist for Waterloo; Assistant Surgeon Medical Reserve Corps, U. S. N. 508 South St., Waterloo, Iowa.

1913. McCrae, Thomas, B.A., M.D., F.R.C.P. (Lond.), Professor of Medicine in the Jefferson Medical College; Physician to the Jefferson and Pennsylvania Hospitals. 1627 Spruce Street.

1895. McFarland, Joseph, M.D., Sc.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College; Pathologist to the Medico-Chirurgical Hospital and to the Philadelphia General Hospital. 442 W. Stafford St., Germantown.

1913. McGlinn, John A., B.A., M.D., Assistant Professor of Obstetrics in the Medico-Chirurgical College; Assistant Obstetrician to the Medico-Chirurgical Hospital; Gynecologist to St. Agnes' Hospital. 113 S. Twentieth St.

ELECTED

1905. McKenzie, Robert Tait, A.B., M.D., Professor of Physical Education and Director of the Department of Physical Education in the University of Pennsylvania. 26 S. Twenty-first St.

1915. McLean, John D., M.D. 1538 S. Broad St.

*1900. McReynolds, Robert Phillips, M.D. 213 S. Broadway, Los Angeles, Cal.

1886. MacCoy, Alexander W., M.D. Consulting Laryngologist to the Bryn Mawr Hospital. 216 S. Fifteenth St.

1910. MacKinney, William H., M.D., Assistant Surgeon to the Dispensary for Genito-urinary Diseases, University Hospital; Assistant in the Urological Dispensary of the German Hospital. 1701 Chestnut St.

1914. Maier, F. Hurst, M.D., Associate in Gynecology to the Jefferson Medical College; Gynecologist to St. Joseph's Hospital. 2035 Chestnut St.

1913. Major, C. Percy, M.D., Physician to the Dispensary of the Germantown Hospital; Pediatrist to the Dispensary of the Germantown Hospital; Pediatrist to the Abington Memorial Hospital. Tenth and Oak Lane.

1896. Makuen, G. Hudson, M.D., Professor of Defects of Speech in the Philadelphia Polyclinic; Consultant Laryngologist and Otologist to the Roosevelt and Frederick Douglass Hospitals; Consultant on Defects of Speech to the New Jersey Training School for Feeble-minded Children. 1627 Walnut Street.

1913. Manges, Willis F., M.D., Röntgenologist to the Jefferson Hospital; Director of the Röntgen Ray Laboratory in the Philadelphia General Hospital. 264 S. Sixteenth St.

1898. Marshall, George Morley, M.D., Laryngologist to the Philadelphia General Hospital; Laryngologist and Otologist to St. Joseph's Hospital. 1819 Spruce St.

1893. Marshall, John, M.D., Nat.Sc.D. (Tübingen), LL.D. Professor of Chemistry and Toxicology in the University of Pennsylvania. 1718 Pine St.

1889. Martin, Edward, M.D., John Rhea Barton Professor of Surgery in the University of Pennsylvania; Surgeon to the University, Howard, Philadelphia General, and Bryn Mawr Hospitals. 1506 Locust St.

1885. Mays, Thomas J., M.D. 1829 Spruce St.

*1868. Mears, J. Ewing, A.M., M.D., LL.D. 1535 Land Title Building, Broad and Sansom Sts.

ELECTED

1911. Meigs, Edward Browning, A.B., M.D., Physiologist in the Dairy Division of the United States Department of Agriculture. 1722 H St., N. W., Washington, D. C.

1914. Mencke, J. Bernhard, A.B., M.D., Assistant Surgeon to the Out-patient Department of the German Hospital; Assistant Surgeon to the Stetson Hospital. 908 N. Sixteenth Street.

1914. Merrill, Wm. Jackson, M.D., 1927 Chestnut St.

*1894. Miller, D. J. Milton, M.D., Associate Physician to the Children's Hospital. 127 S. Illinois Ave., Atlantic City, N. J.

1910. Miller, Morris Booth, M.D., Professor of Surgery in the Philadelphia Polyclinic; Surgeon to the Douglass Memorial Hospital; Assistant Surgeon to the Philadelphia General Hospital. 2117 Pine St.

1881. Mills, Charles K., M.D., Professor of Neurology in University of Pennsylvania; Neurologist to Philadelphia General Hospital; Consulting Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1909 Chestnut Street.

1904. Mitchell, Charles F., M.D., Surgeon to the Germantown, Bryn Mawr, and Chestnut Hill Hospitals, and to the Out-patient Department of the Pennsylvania Hospital. 342 S. Fifteenth St.

†1888. Mitchell, John K., M.D., Attending Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases; Assistant Neurologist to the Presbyterian Hospital; Attending Physician to the Pennsylvania Training School for Feeble-minded Children. 1730 Spruce St.

1908. Montgomery, Charles M., A.B., M.D., Instructor in the Henry Phipps Institute (University of Pennsylvania); Physician to the Dispensaries of the Pennsylvania and St. Agnes' Hospitals. 2210 Locust St.

1882. Montgomery, Edward E., A.M., M.D., LL.D., Professor of Gynecology in the Jefferson Medical College; Gynecologist to the Jefferson Medical College Hospital and to St. Joseph's Hospital. 1426 Spruce St.

1886. Morris, Caspar, M.D. 2050 Locust St.

1893. Morris, Elliston J., M.D., Physician to the Episcopal Hospital and to the Midnight Mission. 128 S. Eighteenth St.

1883. Morris, Henry, M.D., Professor of Anatomy in the Woman's Medical College of Pennsylvania; Senior Visiting Physician to St. Joseph's Hospital. 313 S. Sixteenth St.

ELECTED

1856. Morris, J. Cheston, M.D. 1514 Spruce St.

1906. Morrison, William H., M.D. 8021 Frankford Ave.

1897. Morton, Samuel W., M.D. 1933 Chestnut St.

1905. Müller, George P., M.D., Associate in Surgery in the University of Pennsylvania; Assistant Surgeon to the University Hospital; Professor of Surgery in the Philadelphia Polyclinic; Surgeon to St. Agnes' Hospital; Consulting Surgeon to the Chester County Hospital. 1729 Pine St.

1915. Musser, John H., Jr., B.S., M.D., Associate in Medicine in the University of Pennsylvania; Physician to the Philadelphia General Hospital; Physician in Charge, Medical Dispensary, University Hospital; Dispensary Chief and Assistant in the Presbyterian Hospital. 121 S. Twentieth Street.

1905. Mutschler, Louis H., M.D., Surgeon to the Episcopal Hospital; Assistant Surgeon to the Orthopædic Hospital. 2030 Tioga St.

1896. Myers, T. D., M.D. 1521 Spruce St.

1902. Nassau, Charles F., M.D., LL.D., Assistant Professor of Surgery in the Jefferson Medical College; Surgeon to St. Joseph's Hospital; Consulting Surgeon to the Frankford Hospital; Assistant Surgeon to the Jefferson Medical College Hospital. 1831 Chestnut St.

1886. Neff, Joseph S., A.M., M.D., LL.D., D.P.H. Narbeth, Pa.

1887. Neilson, Thomas Rundle, A.M., M.D., Surgeon to the Episcopal Hospital and to St. Christopher's Hospital for Children; Professor of Genito-urinary Diseases in the University of Pennsylvania. 1937 Chestnut St.

1905. Newcomet, William S., M.D. 3501 Baring St.

1905. Newlin, Arthur, B.S., M.D., Physician to the Pennsylvania Hospital; Physician to the Dispensary of the Children's Hospital; Assistant Physician to the Orthopædic Hospital. 1804 Pine St.

1899. Nicholson, William Rufus, A.B., M.D., Gynecologist to the Polyclinic and Methodist Episcopal Hospitals; Obstetrician to the Presbyterian Hospital; Associate in Obstetrics in the University of Pennsylvania. 1731 Pine St.

*1889. Noble, Charles P., M.D. Chestertown, Md.

1898. Nolan, Edward J., M.D., Recording Secretary and Librarian of the Academy of Natural Sciences of Philadelphia. 825 N. Twentieth St.

ELECTED

1905. Norris, Charles C., M.D., Instructor in Gynecology in the University of Pennsylvania; Physician to the Maternity Hospital; Consultant Gynecologist and Obstetrician to the Henry Phipps Institute of the University of Pennsylvania; Assistant Gynecologist to the University Hospital. 1503 Locust St.

1905. Norris, George William, A.B., M.D., Assistant Professor of Medicine in the University of Pennsylvania; Physician to the Pennsylvania Hospital; Assistant Physician to the University Hospital. 1530 Locust St.

*1901. Norris, Henry, M.D., Surgeon to the Rutherford Hospital. Rutherfordton, N. C.

*1865. Norris, Isaac, M.D. Fairhill, Bryn Mawr, Pa.

1892. Norris, Richard C., M.D., Lecturer on Clinical and Operative Obstetrics in the University of Pennsylvania; Obstetrician in Charge of the Preston Retreat; Visiting Obstetrician to the Philadelphia General Hospital; Gynecologist to the Methodist Episcopal Hospital, and Consulting Obstetrician and Attending Gynecologist to the Southeastern Dispensary and Hospital. 500 N. Twentieth St.

1913. O'Neal, Alexander H., A.B., A.M., M.D., Physician to the Cathcart and Richardson Homes, Devon; Anesthetizer to the Bryn Mawr Hospital. Wayne, Pa.

*1885. Osler, Sir William, Bart., M.D., Regius Professor of Medicine in Oxford University, England. No. 7, Norham Gardens, Oxford, England.

1903. Ostheimer, Maurice, M.D., Associate in Pediatrics in the University of Pennsylvania; Physician-in-Charge of the Children's Dispensary and Assistant Visiting Pediatric Physician, University Hospital; Physician to the Medical Dispensary of Children's Hospital. 2202 De Lancey St.

1913. Outerbridge, George W., A.B., M.D., Instructor in Gynecology and in Surgical Pathology in the University of Pennsylvania; Assistant Gynecologist to the Methodist Hospital and Assistant Surgeon to the Gynecean Hospital. 2040 Chestnut St.

1915. Owen, Hubley R., M.D., Surgeon to the Philadelphia General Hospital; Assistant Surgeon to the Orthopædic Hospital; Chief Surgeon of the Bureaus of Police and Fire, Philadelphia; Assistant Surgeon of the Medical Reserve Corps of the U. S. Navy. 2046 Pine St.

ELECTED

1897. Packard, Francis R., M.D., Surgeon to the Out-patient Department for Diseases of the Ear, Throat, and Nose of the Pennsylvania Hospital; Laryngologist to the Children's Hospital of Philadelphia; Consulting Aurist to the Bryn Mawr Hospital. 304 S. Nineteenth St.

1898. Page, Henry F., M.D., Assistant Physician to the German Hospital and Physician to the Medical Dispensary of the same; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania. 315 S. Sixteenth St.

1906. Pancoast, Henry K., M.D., Professor of Röntgenology in the University of Pennsylvania and Röntgenologist to the University Hospital. Bala, Pa.

1909. Parish, Benjamin D., B.S., M.D., Assistant Instructor in Otology in the University of Pennsylvania; Assistant Surgeon to the Dispensary for Diseases of the Ear, University Hospital; Aurist and Laryngologist to St. Agnes' Hospital. 29 S. Nineteenth St.

1899. Parke, William E., M.D., Consulting Obstetrician to the Episcopal Hospital; Associate Surgeon to the Kensington Hospital for Women; Gynecologist to the Frankford Hospital. 1739 N. Seventeenth St.

1910. Patterson, Ross Vernet, M.D., Assistant Professor of Medicine in the Jefferson Medical College; Assistant Physician to the Jefferson Hospital. 340 S. Sixteenth St.

1903. Pearce, Richard M., M.D., Sc.D., Professor of Research Medicine in the University of Pennsylvania. 2114 De Lancey Place.

1909. Pemberton, Ralph, M.S., M.D., Visiting Physician to the Presbyterian Hospital; Director of the Department of Clinical Chemistry in the Pathological Laboratory of the Presbyterian Hospital. 2224 Locust St.

†1889. Penrose, Charles Bingham, M.D., Ph.D. (Harvard), Formerly Professor of Gynecology in the University of Pennsylvania. 1720 Spruce St.

1914. Pepper, O. H. Perry, B.S. (Univ. of Penna.), M.D. 1811 Spruce St.

†1902. Pepper, William, M.D., Dean of the School of Medicine, and Assistant Professor of Clinical Pathology in the University of Pennsylvania; Physician to the Philadelphia General Hospital; Assistant Physician to the University Hospital. 1811 Spruce St.

ELECTED

1912. Petty, Orlando H., B.S., A.M., M.D., Instructor in Medicine in the Jefferson Medical College; Pathologist and Assistant Physician to St. Timothy's Hospital; Physician to the Kensington Dispensary for the Treatment of Tuberculosis. 6215 Ridge Ave.

1905. Pfahler, George E., M.D., Director of the Röntgen Ray Laboratory of Medico-Chirurgical Hospital. 1321 Spruce St.

1915. Pfeiffer, Damon B., A.B., M.D., Instructor in Surgery, University of Pennsylvania; Assistant Surgeon, University Hospital; Pathologist to the German Hospital; Director of the Clinical Laboratory, Presbyterian Hospital. 2028 Pine St.

1907. Pfromm, George W., Ph.G., M.D., Assistant Physician to the American Stomach Hospital; Consulting Physician to the German Protestant Home for the Aged. 1431 N. Fifteenth St.

1907. Phillips, Horace, M.D., Second Assistant Physician to the Pennsylvania Hospital for the Insane; Visiting Physician to the Eastern Penitentiary of Pennsylvania. Pennsylvania Hospital for the Insane, Forty-fourth and Market Sts.

1911. Physick, Emlen, M.D. Cape May, N. J.

1883. Piersol, George A., M.D., Sc.D., Professor of Anatomy in the University of Pennsylvania. 4724 Chester Ave.

1911. Piersol, George Morris, B.S., M.D., Associate in Medicine in the University of Pennsylvania; Physician to the Episcopal Hospital; Assistant Physician to the University Hospital; Assistant Physician to the Philadelphia General Hospital. 1913 Spruce St.

1905. Pitfield, Robert L., M.D., Pathologist to the Germantown Hospital; Bacteriologist to the Chestnut Hill Hospital for Lung Diseases. 5211 Wayne Ave.

1896. Posey, William Campbell, M.D., Surgeon to the Wills Eye Hospital; Professor of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmic Surgeon to the Howard Hospital; Ophthalmologist to the Pennsylvania Hospital for Epileptics. 2049 Chestnut St.

1899. Potts, Charles S., M.D., Professor of Neurology in the Medico-Chirurgical College; Neurologist to the Philadelphia General Hospital; Consultant to the Insane Department of the Philadelphia General Hospital; Consultant to the Hospital for the Insane, Atlantic County, New Jersey. 2018 Chestnut St.

ELECTED

1907. Price, George E., M.D., Associate Professor of Nervous and Mental Diseases in the Jefferson Medical College; Neurologist to the Philadelphia General Hospital. 1800 S. Rittenhouse Square.

†1903. Pyle, Walter L., A.M., M.D., Assistant Surgeon to the Wills Eye Hospital. 1931 Chestnut St.

1908. Radcliffe, McCluney, A.M. (Lafayette), M.D., LL.D., Ophthalmic Surgeon to the Presbyterian Hospital; Attending Surgeon to the Wills Eye Hospital. 1906 Chestnut St.

1913. Randall, Alexander, A.M., M.D., Assistant Instructor in Surgery in the University of Pennsylvania; Assistant Surgeon in the Genito-Urinary Dispensary of the University of Pennsylvania. Professional Building, Room 401.

1887. Randall, B. Alexander, M.A., M.D., Professor of Otology in the University of Pennsylvania; Ear Surgeon to the Children's Hospital; Consulting Aurist to the Pennsylvania Institution for the Deaf and Dumb, and to St. Timothy's Hospital. 1717 Locust St.

*1904. Ravenel, Mazyck P., M.D., Professor of Preventive Medicine and Bacteriology and Director of the Public Health Laboratory at the University of Missouri, Columbia, Mo.

1897. Rhein, John H. W., M.D., Professor of Diseases of the Mind and Nervous System in the Philadelphia Polyclinic and College for Graduates in Medicine; Neurologist to the Howard Hospital; Physician to the Philadelphia Home for Incurables; Bacteriologist to the Pennsylvania Training School for Feeble-minded Children. 1732 Pine St.

1906. Rhein, Robert D., M.D., Chief Physician to the Clinic of the American Hospital for Diseases of the Stomach; Physician to the Philadelphia Home for Incurables; Examining Physician to the White Haven Sanatorium. 2016 Pine Street.

1891. Rhoads, Edward G., M.D. 159 W. Coulter St., Germantown.

1910. Rhoads, Samuel, M.D., Visiting Physician to the Tuberculosis Department of the Philadelphia General Hospital; Consulting Physician to the Germantown Hospital. 152 Schoolhouse Lane, Germantown.

1898. Riesman, David, M.D., Professor of Clinical Medicine in the University of Pennsylvania; Professor of Clinical Medicine in the Philadelphia Polyclinic; Physician to the Philadelphia General and the Jewish Hospitals. 1715 Spruce St.

ELECTED

1895. Ring, G. Oram, A.M., M.D., Ophthalmic Surgeon to the Episcopal Hospital; Ophthalmologist to the Widener Memorial Home for Crippled Children; Consulting Ophthalmologist to the American Oncologic Hospital. 2014 Chestnut St.

*1905. Risley, J. Norman, M.D., Assistant Surgeon to the Wills Eye Hospital; Ophthalmologist to the Pennsylvania Training School for Feeble-minded Children. 36 Seventh St., New Bedford, Mass.

1891. Risley, S. D., A.M., M.D., Ph.D., Attending Surgeon to the Wills Eye Hospital; Professor (Emeritus) of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Alumnus Manager of the Univeristy Hospital. 2018 Chestnut St.

†1878. Roberts, John B., M.D., Professor of Surgery in the Philadelphia Polyclinic. 313 S. Seventeenth St.

1899. Roberts, Walter, M.D., Professor of Otology in the Philadelphia Polyclinic; Otologist to the Methodist Episcopal Hospital; Laryngologist to the Philadelphia General Hospital. 1732 Spruce St.

1903. Robertson, William Egbert, M.D., Professor of Theory and Practice of Medicine and of Clinical Medicine in Temple University; Physician to the Episcopal, Samaritan, and Garretson Hospitals. 327 S. Seventeenth St.

1902. Robinson, James Weir, M.D., Assistant Surgeon to the Presbyterian Hospital. 326 S. Sixteenth St.

1903. Robinson, William Duffield, Ph.G., M.D. 2012 Mount Vernon St.

1912. Rodman, John Stewart, M.D., Lecturer on Surgery in the Medico-Chirurgical College; Assistant Surgeon to the Medico-Chirurgical Hospital; Surgeon to the Dispensary of the Presbyterian Hospital; Assistant Surgeon to the Out-patient Department of the Pennsylvania Hospital. 2106 Walnut St.

1900. Rodman, William L., M.D., Professor of Surgery in the Medico-Chirurgical College; Surgeon to the Presbyterian Hospital; Surgeon to the Philadelphia General Hospital. 2106 Walnut St.

1909. Rosenberger, Randle C., M.D., Professor of Hygiene and Bacteriology in the Jefferson Medical College; Professor of Hygiene and Preventive Medicine in the Woman's Medical College of Pennsylvania; Director of the Clinical Laboratory of the Philadelphia General Hospital. 2330 N. Thirteenth St.

ELECTED

1898. Ross, George G., M.D., Assistant Surgeon to the German Hospital and Surgeon to the Out-patient Department of the same; Surgeon to the Germantown Hospital; Surgeon to the Stetson Hospital; Instructor in Surgery in the University of Pennsylvania. 1721 Spruce St.

*1907. Royer, B. Franklin, M.D. Donaldson Bldg., Harrisburg, Pa.

†1905. Rugh, James Torrance, A.B., M.D., Clinical Professor of Orthopedic Surgery in the Woman's Medical College of Pennsylvania; Orthopedic Surgeon to the Jefferson Medical College; Orthopedic Surgeon to the Methodist and the Philadelphia General Hospitals. 1616 Spruce St.

1897. Sailer, Joseph, Ph.B., M.D., Professor of Clinical Medicine in Universtiy of Pennsylvania; Physician to the Philadelphia, the University, and Presbyterian Hospitals. 1830 Spruce St.

1900. Sajous, Charles E. de M., M.D., B.Lett., LL.D., Knight of the Legion of Honor, and Officer of the Academy of France; Corresponding Member of the Society of Public Medicine of Belgium. 2043 Walnut St.

1905. Sartain, Paul J., M.D. 212 W. Logan Square.

1908. Sautter, Albert C., M.D., Assistant in the Dispensary for Diseases of the Eye in the University Hospital; Assistant in the Eye Dispensary of the German Hospital. 1421 Locust St.

1906. Saylor, Edwin S., M.D., Chief Ophthalmic Surgeon to the Charity Hospital of Philadelphia, and to the Department Eye and Ear, American Hospital for Diseases of the Stomach. 2005 Chestnut St.

*1910. Scarlet, Rufus B., M.D., Laryngologist to the Home for Consumptives at Chestnut Hill; Assistant in the Department for Diseases of the Ear, Throat, and Nose of the Pennsylvania Hospital; Instructor in Diseases of the Nose and Throat in the Philadelphia Polyclinic and College for Graduates in Medicine. 78 N. Clinton Ave., Trenton, N. J.

1899. Schamberg, Jay F., M.D., Professor of Dermatology and Infectious Eruptive Diseases in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Physician to the Municipal Hospital for Infectious Diseases. 1922 Spruce St.

1887. de Schweinitz, George Edmund, A.M., M.D., LL.D., Professor of Ophthalmology in the University of Pennsylvania; Consulting Ophthalmic Surgeon to the Orthopædic

ELECTED

Hospital and Infirmary for Nervous Diseases; The Philadelphia Polyclinic and School for Graduates in Medicine, and the Philadelphia General Hospital; Ophthalmic Surgeon to the University Hospital. 1705 Walnut St

1913. DE SCHWEINITZ, GEORGE LORD, B.S., M.D., Assistant Surgeon in the Eye Dispensary of the University Hospital; Ophthalmologist to the Haddock Memorial Home; Ophthalmologist to the Williamson School. 2040 Chestnut St.

1910. SCHWENK, PETER N. K., M.A., M.D., Attending Surgeon to the Eye Department of the Pennsylvania Hospital; Attending Surgeon to the Wills Eye Hospital. 1417 N. Broad Street.

1892. SEISS, RALPH W., M.D., Professor of Otology in the Philadelphia Polyclinic; Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb. 255 S. Seventeenth St.

1908. SHANNON, CHARLES E. G., A.B., M.D., Instructor in Ophthalmology in the Jefferson Medical College; Assistant in the Ophthalmological Clinic at the Jefferson Medical College Hospital; Ophthalmologist to the Seybert Institution. 1633 Spruce St.

1897. SHARPLESS, WILLIAM T., M.D., Physician to the Chester County Hospital. West Chester, Pa.

1906. SHIELDS, WILLIAM G., M.D., Dermatologist to Germantown Hospital; Chief of Dermatological Clinic and Assistant Physician to the Jewish Hospital. 414 School Lane, Germantown.

1890. SHOEMAKER, GEORGE ERETY, A.M., M.D., Gynecologist to the Presbyterian Hospital and to the Pennsylvania Epileptic Hospital and Colony Farm. 1831 Chestnut St.

*1908. SHOEMAKER, HARLAN, A.B., M.D., Lecturer in Surgery, University of Southern California, Surgeon to Los Angeles County Hospital, Surgeon to Washington Street Clinic. 621 Marsh Strong Building, Los Angeles, Cal.

†1893. SHOEMAKER, HARVEY, M.D., Visiting Physician to the Sheltering Arms; Consulting Physician to the Southern Home for Destitute Children; Assistant Physician to the German Hospital; Physician to the Out-patient Department of the German Hospital. 2011 Chestnut St.

†1896. SHOEMAKER, WILLIAM T., M.D., Associate Clinical Professor of Ophthalmology in the Woman's Medical College of Pennsylvania; Ophthalmic Surgeon to the Germantown and German Hospitals; Attending Surgeon to the

ELECTED

Eye Department of the Pennsylvania Hospital; Consult ing Ophthalmologist to the Pennsylvania Institution for th Deaf and Dumb, and to the Southern Home for Destitut Children. 109 S. Twentieth St.

1900. Shumway, Edward Adams, B.S., M.D., Ophthalmic Surgeo to the Philadelphia General Hospital; Ophthalmic Surgeo to the Children's Hospital; Instructor in Ophthalmolog in the University of Pennsylvania, and Assistant Ophthalmi Surgeon to the University Hospital; Ophthalmic Surgeo to the German Hospital. 2007 Chestnut St.

1903. Sinclair, John Falconer, M.D., Physician to the Medica Dispensary of the Presbyterian Hospital; Physician to th Philadelphia Orphan Asylum and to the Presbyteria Orphanage; Physician to the Home of the Merciful Saviou for Crippled Children. 4103 Walnut St.

1907. Sinkler, Francis Wharton, A.B., M.D., Physician to th Orthopædic Hospital and Infirmary for Nervous Diseases Physician to the Episcopal Hospital. 1606 Walnut St.

1902. Siter, E. Hollingsworth, M.D., Instructor in Genito urinary Diseases in the University of Pennsylvania; Genito urinary Surgeon to the Philadelphia General Hospital Surgeon-in-Charge of the Genito-urinary Dispensary o the University Hospital; Consulting Genito-Urinary Sur geon to the Eastern Penitentiary, and to the Philadelphi County Prison. 1818 S. Rittenhouse Square.

1904. Skillern, Penn-Gaskell, M.D. 241 S. Thirteenth St.

1904. Smith, Allen J., A.M., M.D., Sc.D. (Penna. Coll.), LL.D (McGill Univ.), Professor of Pathology and of Comparativ Pathology, and Director of Courses in Tropical Medicin in the University of Pennsylvania. Medical Laboratories University of Pennsylvania.

1905. Smith, S. MacCuen, M.D., Professor of Otology in th Jefferson Medical College; Aurist and Laryngologist to th Germantown Hospital; Aurist to the Jewish Hospital; Con sulting Aurist to the Oncologic Hospital. 1429 Spruce St.

1908. Speese, John, M.D., Instructor in Surgery and Surgica Pathology in the University of Pennsylvania; Associate i Surgery in the Philadelphia Polyclinic; Surgeon to th Children's Hospital; Assistant Surgeon to the Presbyteria and Polyclinic Hospitals. 2206 Locust St.

1895. Spellissy, Joseph M., A.M., M.D., Visiting Surgeon to St Joseph's and to the Methodist Episcopal Hospitals; Assistan

ELECTED

Surgeon to the Orthopedic Department of the University Hospital. 110 S. Eighteenth St.

1897. Spiller, William G., M.D., Professor of Neurology in the University of Pennsylvania; Clinical Professor of Nervous Diseases in the Woman's Medical College of Pennsylvania; Neurologist to the Philadelphia General Hospital; Consultant Neurologist to the Pennsylvania Hospital. 4409 Pine St.

1894. Stahl, B. Franklin, B.S., Ph.G., M.D., Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania; Associate in Medicine and Lecturer on Dietetics of the Sick in the University of Pennsylvania; Visiting Physician to St. Agnes' and the Philadelphia General Hospitals. 1727 Pine St.

1909. Starbuck, J. Clinton, M.D. 42 E. Washington St., Media, Pa.

*1875. Starr, Louis, M.D., LL.D. (Haverford). The Vanderbilt Hotel, 34th St. and Park Ave., New York City.

1912. Stauffer, Nathan Pennypacker, D.D.S., M.D., Laryngologist and Otologist to the Dispensary of the Presbyterian Hospital; to the Pennsylvania Hospital; to the Philadelphia General Hospital, Tubercular Department; to the Home for Crippled Children. 218 S. Twentieth St.

1910. Stellwagen, Thomas C., Jr., M.D., Chief Clinical Assistant in the Out-patient Surgical Department of the Jefferson Medical College Hospital. 110 S. Nineteenth St.

1884. Stelwagon, Henry W., M.D., Ph.D., Professor of Dermatology in the Jefferson Medical College. 1634 Spruce St.

1895. Stengel, Alfred, M.D., Sc.D., Professor of Medicine in the University of Pennsylvania; Physician to the University Hospital and the Pennsylvania Hospital. 1728 Spruce Street.

1901. Stevens, Arthur A., M.D., Professor of Materia Medica, Therapeutics, and Clinical Medicine in the Woman's Medical College of Pennsylvania; Lecturer on Physical Diagnosis in the University of Pennsylvania; Physician to the Episcopal and St. Agnes' Hospitals. 314 S. Sixteenth St.

1902. Stewart, Francis T., M.D., Professor of Clinical Surgery in the Jefferson Medical College; Surgeon to the Germantown Hospital; Surgeon to the Out-patient Department of the Pennsylvania Hospital. 311 S. Twelfth St.

1914. Stewart, Thomas S., B.S. (Univ. of Penna.), M.D. 301 S. Eighteenth St.

ELECTED

1898. Stout, George C., M.D., Professor of Otology in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist and Aurist to the Presbyterian Hospital, the Children's Aid Society, and the William Penn Charter School. 1611 Walnut St.

1884. Stryker, Samuel S., M.D., Physician to the Presbyterian Hospital. 3833 Walnut St.

*1900. Swan, John M., M.D. 457 Park Avenue, Rochester, N. Y.

1898. Sweet, William M., M.D., Clinical Professor of Ophthalmology in the Jefferson Medical College, and Ophthalmic Surgeon to the Jefferson Medical College Hospital; Professor of Diseases of the Eye in the Philadelphia Polyclinic; Attending Surgeon to the Wills Eye Hospital. 1205 Spruce St.

1900. Talley, James Ely, A.B., M.D., Visiting Physician to the Presbyterian and Methodist Episcopal Hospitals; Consulting Physician to the Eastern Penitentiary. 218 S. Twentieth Street.

1911. Taylor, Alonzo Englebert, M.D., Rush Professor of Physiological Chemistry in the University of Pennsylvania. 4522 Locust St.

1886. Taylor, John Madison, A.B. and A.M. (Princeton), M.D., Adjunct Professor of Non-Pharmaceutical Therapeutics in the Temple University; Editor *Monthly Cyclopedia of Practical Medicine;* Consulting Physician to the Elwyn, Pa., and the Vineland, N. J., Training Schools for Feeble-minded Children. 1504 Pine St.

1887. Taylor, William J., M.D., Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases, and to St. Agnes' Hospital; Consulting Surgeon to the West Philadelphia Hospital for Women. 1825 Pine St.

1886. Taylor, William L., M.D. 1340 N. Twelfth St.

†1910. Thomas, Benjamin A., A.M., M.D., Professor of Genito-urinary Surgery in the Philadelphia Polyclinic and College for Graduates in Medicine; Instructor in Surgery in the University of Pennsylvania; Surgeon-in-Chief to the Out-patient Department of the University Hospital. 116 S. Nineteenth St.

1867. Thomas, Charles Hermon, M.D. 3634 Chestnut St.

1912. Thomas, Frank Wister, A.M., M.D., Visiting Physician to "Buttercup Cottage;" Consulting Physician to the Germantown Hospital. 27 E. Mt. Airy Ave.

ELECTED

1907. Thomas, Thomas Turner, M.D., Associate Professor of Applied Anatomy, and Associate in Surgery in the University of Pennsylvania; Surgeon to the Philadelphia General Hospital; Assistant Surgeon to the University Hospital. 2005 Chestnut St.

1897. Thomson, A. G., M.D., Ophthalmic Surgeon to the Pennsylvania Railroad Company. 724 Stock Exchange Bldg.

1896. Thorington, James, A.M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmic Surgeon to the Presbyterian Hospital; Ophthalmologist to the Ellwyn, Pa., Training School for Feeble-minded Children. 2031 Chestnut St.

1898. Thornton, Edward Q., M.D., Assistant Professor of Materia Medica in the Jefferson Medical College. 1331 Pine St.

1912. Torrey, Robert G., M.D., Assistant Physician to the Philadelphia General Hospital; Physician to the State Tuberculosis Dispensary. 1716 Locust St.

1896. Toulmin, Harry, M.D., Medical Director of the Penn Mutual Life Insurance Company. 925 Chestnut St.

1908. Tracy, Stephen E., M.D., Gynecologist to the Stetson Hospital. 1527 Spruce St.

1901. Tucker, Henry, M.D., Genito-urinary Surgeon to the Philadelphia General Hospital; Curator of the Academy of Natural Sciences of Philadelphia. 2000 Pine St.

†1894. Tunis, Joseph Price, M.D., Clinical Assistant to the Nose and Throat Dispensary of the Polyclinic Hospital. St. Martin's, Philadelphia.

1901. Turner, John B., M.D. 1833 Chestnut St.

1866. Tyson, James, M.D., LL.D., Emeritus Professor of Medicine in the University of Pennsylvania and late Physician to the Hospital of the University of Pennsylvania, and to the Pennsylvania Hospital. 1506 Spruce St.

1897. Tyson, T. Mellor, M.D., Physician to the Philadelphia General Hospital; Physician to the Rush Hospital, the Philadelphia Lying-in-Charity Hospital, and the Children's Aid Society of Philadelphia. 1506 Spruce St.

1904. Uhle, Alexander A., M.D., Assistant Instructor in Genito-urinary Diseases in the University of Pennsylvania; Assistant Surgeon to the Dispensary for Genito-urinary Diseases, University Hospital; Assistant Genito-urinary Surgeon to the Philadelphia General Hospital; Assistant Surgeon to the Dispensary of the German Hospital. 1701 Chestnut St.

ELECTED

1907. Ullom, Josephus Tucker, M.A., M.D., Member of the Staff of the Henry Phipps Institute, Visiting Physician to the Chestnut Hill Hospital. 24 Carpenter St., Germantown.

1913. Vail, William Penn., B.S., M.S., M.D., Laryngologist to the Pennsylvania Institution for the Instruction of the Blind; Laryngologist to the Department for Tuberculosis of the Philadelphia General Hospital; Otolaryngologist to the Douglass Hospital; Assistant Laryngologist and Otologist to the Out-patient Department of the Pennsylvania Hospital; Assistant Laryngologist to the Children's Hospital. 1700 Walnut St.

1873. Van Harlingen, Arthur, Ph.B. (Yale), M.D., Emeritus Professor of Diseases of the Skin in the Philadelphia Polyclinic; Dermatologist to the Children's Hospital. 1831 Chestnut St.

1903. Van Pelt, William Turner, M.D. Consulting Ophthalmologist to the Episcopal Hospital. 1100 Widener Building.

1893. Vansant, Eugene Larue, M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic; Visiting Physician to the Throat, Nose, and Ear Department of the Howard Hospital. 1929 Chestnut St.

1912. Vaux, Norris Wistar, M.D., Surgeon to the Chestnut Hill Hospital; Surgeon to the Dispensary of the Germantown Hospital. 8901 Germantown Ave., Chestnut Hill.

*1897. Veasey, Clarence A., A.M., M.D. Suite 404, Paulsen Building, Spokane, Wash.

†1883. Vinton, Charles Harrod, A.M., M.D. P. O. Box 464, Atlantic City, N. J.

1903. Wadsworth, William Scott, M.D. 207 S. Forty-fifth St.

1906. Walker, John K., M.D., Physician to the Children's Hospital of the Mary J. Drexel Home; Physician to the Out-patient Department of the Pennsylvania Hospital. 1915 Rittenhouse St.

1907. Walker, Warren, M.D., Dermatologist to the Episcopal and Howard Hospitals; Assistant Dermatologist to the Pennsylvania Hospital. 246 S. Twenty-second St.

1904. Walsh, Joseph, A.M., M.D., Visiting Physician to and Medical Director of the White Haven Sanatorium; Medical Director of St. Agnes' Hospital. 736 Pine St.

ELECTED

1910. Ward, E. Tillson, A.M., M.D. 1415 S. Broad St.

*1893. Warren, Joseph W., M.D., Department of Health. Harrisburg, Pa.

1895. Watson, Arthur W., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist to the Jewish Hospital; Laryngologist and Aurist to the Mt. Sinai Hospital; Laryngologist to Home for Incurables. 126 S. Eighteenth Street.

1886. Watson, Edward W., M.D., Physician to the Magdalene Home. 38 S. Nineteenth St.

1903. Weber, Charles H., M.D., Physician to the Dispensary of the Children's Hospital. 2048 Pine St.

1906. Weisenburg, Theodore H., M.D., Professor of Clinical Neurology and of Neuropathology in the Medico-Chirurgical College; Neurologist to the Philadelphia General Hospital; Consulting Neurologist to the State Hospital for the Insane at Norristown, and to the State Hospital for the Feeble-minded and Epileptic at Spring City. 2030 Chestnut St.

1883. Welch, William M., M.D., Chief Diagnostician to the Bureau of Health, and Consulting Physician to the Municipal Hospital for Contagious Diseases; Consulting Physician to the Northern Dispensary and the Northern Home for Friendless Children. 1411 Jefferson St.

1913. Wells, P. Frailey, A.M., M.D., Ph.D. S. W. Cor. Fortieth and Brown Sts.

1897. Wells, William H., M.D., Assistant Professor of Obstetrics in the Jefferson Medical College; Assistant Obstetrician to the Jefferson Medical College Hospital; Pediatrician to the Willing Day Nursery; Pediatrician to the Charity Hospital. 1135 Spruce St.

1893. Westcott, Thompson S., M.D., Associate in Diseases of Children in the University of Pennsylvania; Pediatrist to the Methodist Episcopal Hospital; Assistant Physician to the Children's Hospital; Pediatrist to the Jewish Hospital. 1720 Pine St.

1884. Wharton, Henry R., M.D., Surgeon to the Presbyterian and the Children's Hospitals; Surgeon to Girard College; Consulting Surgeon to the Bryn Mawr Hospital, the Chestnut Hill Hospital, St. Christopher's Hospital for Children, the Pennsylvania Institution for the Deaf and Dumb, and the Pennsylvania Institution for the Blind. 1725 Spruce St.

ELECTED

1901. White, Courtland Y., M.D., Director of the Pathological Laboratories of the Episcopal Hospital; Pathologist to the Children's Hospital and to the Kensington Hospital for Women; Chief Bacteriologist to the Bureau of Health, Department of Health and Charities, Philadelphia. 1808 Diamond St.

1878. White, J. William, M.D., Ph.D., LL.D. (Hon., Aberdeen), John Rhea Barton Emeritus Professor of Surgery in the University of Pennsylvania. 1810 S. Rittenhouse Square.

1905. Whiteway, Harold M., M.D. 1924 Chestnut St.

1898. Whiting, Albert D., M.D., Surgeon to the Germantown Hospital; Assistant Surgeon to the German Hospital; Assistant Surgeon to the University Hospital; Instructor in Surgery in the University of Pennsylvania. 1523 Spruce Street.

1914. Willard, de Forest P., B.S. (Univ. of Penna.), M.D. 1933 Chestnut St.

1907. Williams, Carl, B.S., M.D., Ophthalmic Surgeon to the Germantown Hospital; Instructor in Ophthalmology in the University of Pennsylvania; Ophthalmic Surgeon to the Pennsylvania Institution for the Deaf and Dumb. School Lane and Greene Sts., Germantown.

1915. Willits, Charles H., A.M., M.D., Medical Director of the Provident Life and Trust Company. Rittenhouse Hotel, Twenty-second and Chestnut Sts.

1902. Willson, Robert N., M.D., Pathologist to the Presbyterian Hospital; Physician to the Philadelphia General Hospital. 1827 Spruce St.

1881. Wilson, H. Augustus, M.D., Professor of Orthopedic Surgery in the Jefferson Medical College; Emeritus Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Consulting Orthopedic Surgeon to the Philadelphia Lying-in Charity Hospital and the Kensington Hospital for Women; Orthopedic Surgeon to St. Agnes' Hospital. 1611 Spruce Street.

1874. Wilson, James Cornelius, A.M. (Princeton), M.D., Emeritus Professor of the Practice of Medicine and of Clinical Medicine in the Jefferson Medical College; Physician-in-Chief to the German Hospital; Emeritus Physician to the Pennsylvania Hospital; Consulting Physician to the Bryn Mawr Hospital. 1509 Walnut St.

1902. Wilson, Samuel M., M.D. 1517 Arch St.

ELECTED

1897. Wilson, W. Reynolds, M.D. 1709 Spruce St.

1912. Winsor, Henry, M.D., Surgeon to the Dispensary of the Episcopal Hospital; Prosector to the Associate Professor of Applied Anatomy, and Assistant Instructor in Surgery in the University of Pennsylvania. 319 S. Sixteenth St.

1904. Wister, James W., M.D., Physician to the Out-patient Department of the Germantown Hospital. 5430 Germantown Ave.

*1901. Witmer, A. Ferree, M.D. Freeport, Long Island, N. Y.

1893. Wood, Alfred C., M.D., Assistant Professor of Surgery in the University of Pennsylvania; Surgeon to the University, the Philadelphia General, St. Timothy's, and the Howard Hospitals. 2035 Walnut St.

1900. Wood, George B., M.D., Instructor in Laryngology in the University of Pennsylvania; Assistant in the Clinic for Diseases of the Nose and Throat at the Polyclinic Hospital. 129 S. Eighteenth St.

1865. Wood, Horatio C., M.D., LL.D. (Yale and Lafayette), Emeritus Professor of Materia Medica and Therapeutics in the University of Pennsylvania. 4107 Chester Ave.

1903. Wood, Horatio C., Jr., M.D., Professor of Pharmacology and Therapeutics in the Medico-Chirurgical College. 1905 Chestnut St.

1880. Woodbury, Frank, M.D., Secretary to the Committee on Lunacy of the Board of Charities of Pennsylvania. 218 S. Sixteenth St.

*1911. Woods, Andrew H., A.B., M.D., Neurologist to the Canton Hospital and to the Canton Hospital for Women; Acting President and Medical Superintendent of the Canton Christian College. Canton Christian College, Canton, China.

†1897. Woodward, George, M.D. W. Willow Grove Ave., Chestnut Hill, Philadelphia.

1913. Woodward, W. Wellington, M.D. 26 S. Church St., West Chester, Pa.

1903. Worden, Charles B., M.D., Associate in Diseases of the Stomach and Intestines in the Philadelphia Polyclinic; Physician to the Dispensary of the Presbyterian Hospital; Anesthetizer to the Orthopedic Department of the University Hospital; Physician to the Presbyterian Orphanage. 322 S. Sixteenth St.

ELECTED

1889. Young, James K., M.D., Professor of Orthopedic Surgery in the Philadelphia Polyclinic; Clinical Professor of Orthopedic Surgery in the Woman's Medical College of Pennsylvania; Associate Professor of Orthopedic Surgery in the University of Pennsylvania. 222 S. Sixteenth St.

1894. Zentmayer, William, M.D., Professor of Ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine; Attending Surgeon to the Wills Eye Hospital; Ophthalmologist to the Glen Mills School. 1819 Spruce St.

1899. Ziegler, S. Lewis, A.M., M.D., LL.D., Attending Surgeon to the Wills Eye Hospital; Chief Ophthalmic Surgeon to St. Joseph's Hospital; Membre Société Française d'Ophthalmologie; Director of Public Health and Charities of Philadelphia. 1625 Walnut St.

1887. Ziegler, Walter M. L., A.M., M.D. 1418 N. Seventeenth St.

1895. Zimmerman, Mason W., M.D., Consulting Ophthalmic Surgeon to the Germantown Hospital. 1522 Locust St.

ASSOCIATE FELLOWS

(Limited to Fifty, of whom Twenty may be Foreigners)

American

ELECTED

1911. Abbe, Robert, M.D. 13 W. Fiftieth St., New York City, N. Y.

1909. Billings, Frank, M.D., 122 S. Michigan Boulevard, Chicago, Illinois.

1886. Cheever, David W., M.D., 557 Boylston Street, Boston, Massachusetts.

1893. Councilman, William T., M.D., Harvard Medical College, Boston, Massachusetts.

1909. Crile, George W., M.D., 1021 Prospect Avenue, S. E., Cleveland, Ohio.

1909. Dana, Charles Loomis, M.D., 53 West Fifty-third Street, New York City, New York.

1892. Emmet, Thomas Addis, M.D., 91 Madison Avenue, New York City, New York.

1903. Gorgas, William C., M.D., U. S. A., Washington, D. C.

1891. Jacobi, A., M.D., 19 East Forty-seventh Street, New York City, New York.

1912. McCaw, Lieut. Col. Walter D., M.D. Care of Surgeon-General's Office, Washington, D. C.

1909. Mall, Franklin P., M.D., 1514 Bolton Street, Baltimore, Maryland.

1906. Mayo, William J., M.D., Rochester, Minnesota.

1906. Pilcher, Lewis Stephen, M.D., 145 Gates Avenue, Brooklyn, New York.

1886. Reeve, John C., M.D., LL.D., S. W. corner Third and Wilkinson Streets, Dayton, Ohio.

1906. Shattuck, Frederick C., M.D., 135 Marlborough Street, Boston, Massachusetts.

ELECTED

1896. Tiffany, L. McLane, M.D., 831 Park Avenue, Baltimore, Maryland.
1894. Warren, J. Collins, M.D., 58 Beacon Street, Boston, Massachusetts.
1894. Weir, Robert F., M.D., 11 East Fifty-fourth Street, New York City, New York.
1892. Welch, William H., M.D., Johns Hopkins Hospital, Baltimore, Maryland.

Foreign

1890. Baccelli, Guido, Rome, Italy.
1908. Bannerman, W. B., M.D., Lt. Col. I. M. S., 11 Strathearn Place, Edinburgh, Scotland.
1894. Brunton, Sir T. Lauder, M.D., 10 Stratford Place, London, W., England.
1899. Fraser, Sir Thomas R., M.D., LL.D., F.R.C.P., F.R.S., 13 Drumsheigh-Gardens, Edinburgh, Scotland.
1903. Horsley, Sir Victor Alexander Haden, F.R.S., 25 Cavendish Square, London, England.
1893. von Jaksch, Rudolf, M.D., Prague, Bohemia.
1903. Kocher, Prof. Theodor, M.D., Laupenstrasse 25, Berne, Switzerland.
1912. Lazarus, Paul, M.D., Hindersinstr. 2, Berlin, N. W., Germany.
1909. Macallum, Archibald B., M.A., M.B., Ph.D., Sc.D., LL.D., F.R.S., 59 St. George Street, Toronto, Canada.
1906. Myles, Sir Thomas, M.D., 33 Merion Square, W., Dublin, Ireland.
1898. Roddick, Thomas G., M.D., 80 Union Avenue, Montreal, Canada.
1908. Ross, Major Ronald, M.D., R.A., Liverpool School of Tropical Medicine, Liverpool, England.
1869. Valcourt, Th. de, M.D., Cannes, France.
1904. Waldeyer, Prof. Wilhelm, M.D., W. 62 Sutherstr. 35, Berlin, Germany.

CORRESPONDING MEMBERS

1880. Carrow, Flemming, M.D., Washington Arcade, Detroit, Michigan.
1885. Rendu, Jean, M.D., Lyons, France.
1915. McIntire, Charles, M.D., Easton, Pennsylvania.

NECROLOGICAL LIST

FELLOWS

RICHARD FLAVEL WOODS,	February	10, 1915
THOMAS BIDDLE,	February	19, 1915
FRED. HARLEN KLAER,	February	27, 1915
THOMAS HEWSON BRADFORD,	June	25, 1915
JOHN BACON,	August	2, 1915
ALBERT R. MOULTON,	August	16, 1915

ASSOCIATE FELLOWS

CHARLES J. FINLAY,	August	20, 1915
GEORGE M. STERNBERG, U. S. A.,	November	3. 1915

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RENE LAROCHE, M.D.
B 1795 - D 1872
J PERCY KEATING ESQ

REMARKS ON PRESENTATION OF PORTRAIT OF DR. RÉNÉ LA ROCHE[1]

By WILLIAM J. TAYLOR, M.D.

Mr. President and Fellows of the College:

I have the honor and great privilege of presenting to the College, on behalf of Mr. J. Percy Keating, a portrait of his grandfather, Dr. Réné La Roche, who was born in Philadelphia in the year 1795 and died in 1872.

He served as a captain of volunteers in the War of 1812, and was graduated in medicine from the University of Pennsylvania in 1820, and was elected a Fellow of this College in 1827.

He was a member of various learned societies in Philadelphia, the American Philosophical Society, the Academy of Natural Sciences, the Philadelphia County Medical Society, the American Medical Association and the Medical Society of the State of Pennsylvania. He was a member of the Board of Health of Philadelphia and a Trustee of the University of Pennsylvania.

He was a practitioner of medicine of high repute and wrote many interesting papers, particularly one upon pneumonia and its relation to autumnal fevers, and including an inquiry into the existence and morbid agency of malaria (Blanchard & Lea, 1854). He was particularly well known for his writings upon yellow fever.

The name of the artist who painted this portrait is not known, but it was painted for, and owned by, his daughter, who lived for many years in Brussels, and upon her death it was bequeathed Mr. J. Percy Keating, who presents it now to the College.

[1] Read February 3, 1915.

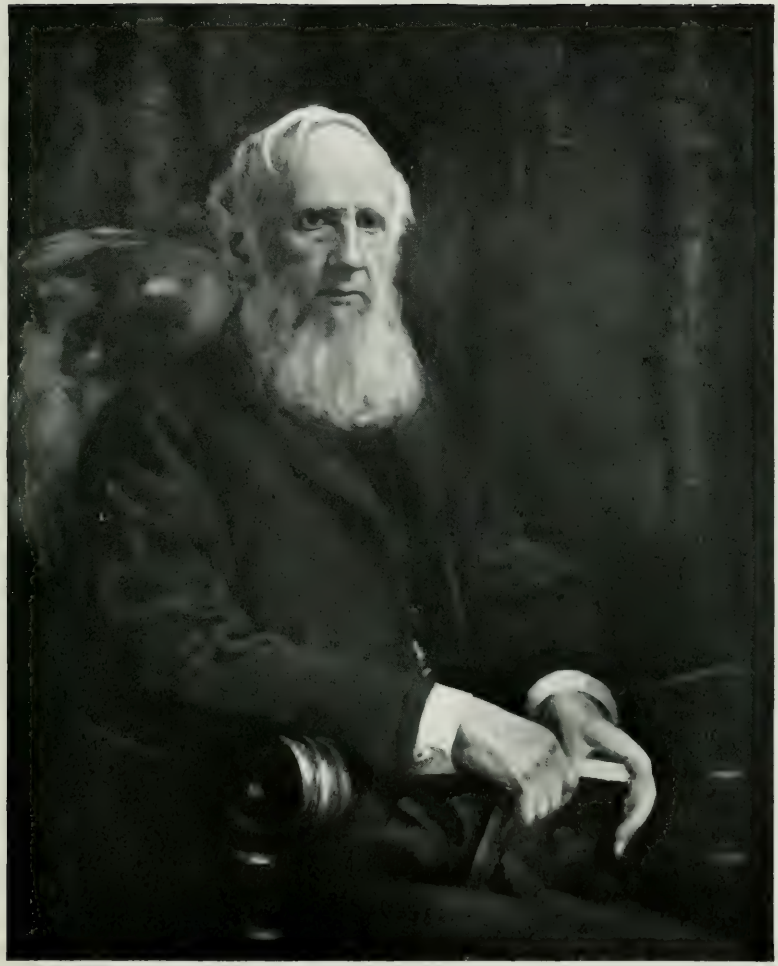
REMARKS ON PRESENTATION OF PORTRAIT OF DR. LOUIS A. DUHRING[1]

By DAVID RIESMAN, M.D.

It is unnecessary, Mr. President and Gentlemen, to dwell at length on the life and achievements of Dr. Louis A. Duhring or to attempt a complete delineation of the remarkable personality which made him conspicuous among men. These things have been done by Dr. Stelwagon in an addresss noteworthy for its fidelity and literary charm. All that remains for me to do is to point out a few of the salient features of Dr. Duhring's life-work, so that it may be understood why this College, so sparing in the bestowal of honors, has singled him out for one of its highest distinctions.

Dr. Duhring belonged to that small group of men who by the originality of their genius have made American medicine international. For a certain period of his life he was of all American physicians probably the one best known abroad. He chose as his special study diseases of the skin, and ranks by the consensus of all as one of the great masters in this field. Not only did he have the highest respect of his patients, but he had something that is not always associated with popularity among the laity, the profound regard of his colleagues. Dr. Duhring's attitude toward his chosen branch showed the philosophic quality of his mind and the breadth of his medical outlook. For him dermatology was but a part of general medicine, a deeply grounded

[1] Read February 3, 1915.



LOUIS A. DUHRING

(From the painting by Hugh H. Breckenridge)

conviction to which he gave definite expression when he called his *magnum opus* not dermatology, but "cutaneous medicine."

Dr. Duhring was not easily approached, but lived detached, silent and serene, keeping from the profane crowd the great plans he was maturing for the benefit of posterity. In his last will he gave to the University of Pennsylvania, of which he was an alumnus and in which he taught for more than a generation's span, a vast fortune to be used in the interest of medical and archeological science, especially in research in his beloved branch of dermatology, and to this College he bequeathed a munificent sum for expanding the usefulness of the Library. In appreciation of his generosity, and to honor his memory, the College has ordered a portrait painted of him to hang forever upon its walls. The committee appointed by you, Mr. President, commissioned Mr. Breckenridge to execute this portrait, and we hope you will find that the artist has succeeded in converting the dull, flat product of the camera into a true and speaking likeness of the man.

And now, in compliance with your own request and that of my colleagues, I unveil the portrait of Dr. Duhring, beneath which might fittingly be inscribed the noble motto of the College, "*Non sibi sed toti.*"

THE ANNUAL ADDRESS OF THE PRESIDENT[1]

By JAMES CORNELIUS WILSON, A.M., M.D.

It will, I trust, be agreeable to you for me to follow in this my second address the usual custom and consider in brief review the affairs of the College during the year that has just come to an end.

At the nine stated meetings held during this period there were present in all 510 Fellows, an average attendance of $56\frac{2}{3}$—a falling off of 17 from that of last year.

Three special meetings were held at the call of the President:

A special meeting on January 6, for the purpose of commemorating with honor and solemnity the death of Dr. S. Weir Mitchell. Upon this occasion addresses were delivered by Dr. Keen, Dr. Tyson, and Dr. de Schweinitz.

A special meeting March 27, to hear an address by Dr. Gustave Monod, of Vichy, on "The Opportunities for Post-Graduate Study in Medicine in Paris."

A special meeting, in conjunction with the Section on General Medicine, October 12, to hear an address by Thomas Lewis, F.R.C.P., "On the Heart Sounds, with Lantern Demonstrations."

These meetings were largely attended by Fellows of the College and their friends.

In addition to these special meetings there was held in this hall, on March 31, under the auspices of this Institution, your president presiding, in memory of S. Weir Mitchell, a joint meeting of The College of Physicians, The American Philosophical Society,

[1] Read January 6, 1915.

the University of Pennsylvania, the Library Company of Philadelphia, The Jefferson Medical College, and The Academy of Natural Sciences. The speakers on this occasion were Dr. Talcott Williams, of Columbia University, Dr. William H. Welch, of Johns Hopkins University, and Mr. Owen Wister, of Philadelphia. These addresses befitting the purpose of the large gathering of Dr. Mitchell's friends and associates were of unusual earnestness and interest, and the Committee having charge of the arrangements will close its labors by their publication in a suitable memorial volume which is now nearly ready for distribution.

At the regular stated meetings five memoirs of deceased Fellows were read—at the December meeting, a memoir of the late Dr. Charles A. Oliver by Dr. McCluney Radcliffe; at the January meeting, a memoir of the late Dr. Richard A. Cleeman, by Dr. Frederick P. Henry; at the March meeting, a memoir of the late Dr. George McClellan, by Dr. J. Chalmers DaCosta; at the April meeting, a memoir of the late Dr. Arthur V. Meigs, by Dr. Edward B. Meigs, and a memoir of the late Dr. Louis A. Duhring by Dr. Henry W. Stelwagon.

The scientific business has maintained the traditions of the College in representing the most advanced thought in the varied departments of medicine. Nineteen papers based upon critical clinical and laboratory work of general and special interest have been presented during the year. Six speakers not Fellows have by invitation appeared before us. Five of the communications were illustrated by lantern slides. The discussions have been of a high order and contributed greatly to the interest of the meetings.

At the meeting of May 6, the scientific business consisted of "A Symposium on Municipal Hygiene," arranged by the Committee on Public Health and Preventive Medicine. One of the speakers by invitation was Dr. S. Josephine Baker, the Director of the Bureau of Child Hygiene of New York. Her subject was "The Organization of the Bureau of Child Hygiene in New York City and its Results." The communication was of unusual interest and importance and admirably presented. It is to be noted that, as far as our records show, this was the first occasion in the history

of the College on which a woman has presented a formal paper, by invitation, upon the floor of the College. It was received in such a way that we may now be prepared to welcome anyone who has a real message of science or applied science to bring, regardless of sex.

The eighth of the series of Weir Mitchell Lectures was delivered on February 25, 1914, by Dr. Harvey Cushing. The subject was "Clinical Types of Dispituitarism." This discourse was of rare interest, expounding as it did the original views of the speaker and bringing alike the theoretical considerations and the results of the experimental and clinical work fully up to date. It was abundantly illustrated by lantern slides.

The work of the several sections of the College has been carried on with activity and success and the attendance at the meetings has been large.

The Committee on Publication has continued to discharge its laborious duties with full satisfaction to the authors of the papers and the Fellows of the College. Volume XXXV of the Third Series was issued early in 1914. It contained 495 pages, 45 more than Volume XXXIV, and was published at a cost well within the limits of the appropriation.

The report of the Library Committee shows a continuous increase in our books. The total number, including bound volumes and 10,064 unbound "Reports" and "Transactions," is now 105,540. In addition to these there are 12,889 unbound "Theses" and "Dissertations" and 85,142 unbound "Pamphlets." From all sources we received during the year 3977 volumes, 11,587 pamphlets, and 21,158 numbers of journals. The individual donors number 482.

The number of new publications added to the Library during the past year was 797. Of these, 56 were written or edited by Fellows of the College.

The visits paid to the Library during 1914 numbered 8469. Of these visits, 3818 were made by Fellows of the College. The Library was kept open two evenings each week and on the six minor legal holidays.

The number of books consulted of which record was kept was 24,000; the number taken out was 4301. The cataloguing makes steady and satisfactory progress.

The number of photographs received in response to requests sent out by the librarian was: foreign, 86; Fellows of the College, 24.

The total number of periodicals received was 1254, new subscriptions to American journals being 15, and to foreign journals 40.

The study rooms have been in constant use throughout the year, the average number of volumes called for and retained being about 166.

Conditions in Europe due to war have greatly interfered with the publication of foreign works upon medical subjects and particularly with the regular issue of periodicals. This fact and the arrest of travel likely to continue for some time will seriously affect the receipt of French and German publications, and our acquisition of incunabula and other old and rare books.

During the past year the "Library Endowment Funds" have been increased by the Horace Magee Memorial Fund, $15,000; an additional $2000 to the J. Ewing Mears Fund and an additional $87.39 to the William F. Norris Fund.

The total amount of the Library Endowment Funds is now $105,710.13, which yielded last year an income of $4305.24. The general expenditures for the Library amounted to $9405.82.

The following is a list of incunabula, rare medical books, works of special interest, manuscripts, portraits, and other interesting and valuable gifts received by the College during the past year:

Incunabula

(Total number at this date, 176)

Albertus Magnus. (Summa de quatuor coaevis et de homine.) Venetiis, Simon de Luere, 1498. A remarkably well-preserved copy in perfect condition, from the famous "Strozzi" Library. (Presented by Dr. Richard H. Harte.)

Plinius, Cajus Secundus. (Historia naturalis.) Historia naturale di C. Plinio secondo tradocta di lingua Latina in Fiorentina per Christophoro Landino Fiorentino. Venetiis, Nicolaus Janson Gallicus, 1476. A superb copy. Believed to be the first Italian edition of any classic. (Presented by Henry Reed Hatfield, Esq.)

Works of Special Interest

Ayrer, G. H. Commentatio iuris ecclesiastici de iure dispensandi circa connubia. Gottingae, Regiae Univ. off. librar., 1742. (Presented by Dr. Thomas Biddle.)

Briggs, Gulielmus. Ophthalmo-graphia, sive oculi ejusque partium descriptio anatomica. Lugduni Batavorum, 1686. (Presented by Dr. S. Weir Mitchell.)

Chamberlen, Peter. Vindication of publick artificiall baths and bath-stoves. London, 1648. (Presented by Dr. S. Weir Mitchell.)

Chesneau, Nicolas. Observationum medicarum libri quinque. Lugduni Batavorum, Haak, 1719. (By purchase.)

Faber, A. O. De auro potabili medicinali. (London), Faber, 1677. (Fund for rare books.)

Fuller, Henry J. "Old Q" and the apothecary, being a record of a famous trial. (London, privately printed), 1913. (Presented by the author.)

Glauber, J. R. Pharmacopoeae spagyricae. Amstelodami, Janssonium, 1657. (Fund for rare books.)

Harvey, William. Exercitationes de generatione animalium. Londini, Pulleyn, 1651. First edition. A presentation copy from Harvey to Francis Bernard. This work was specially bound for Dr. Mitchell by Emily Tuckerman, with an impression of the Harvey "Stemma" on the sides. (Presented by Dr. John K. Mitchell.)

Hippocrates. Aphorisms of Hippocrates and the sentences of Celsus. Second edition corrected * * * by Sir Conrad Sprengell. London, Wilkin, 1735. (Fund for rare books.)

Letters and memoranda relating to William Harvey. (Bequeathed by Dr. S. Weir Mitchell.)

Mitchell, S. Weir. List of medical cadets in service during the War of the Rebellion. (Philadelphia, 1913). (Typewritten.) (Presented by Dr. S. Weir Mitchell.)

Pamphlets relating to William Harvey, with manuscript notes by W. J. Harvey. (Bequeathed by Dr. S. Weir Mitchell.)

Pemell, Robert. De morbis puerorum, a treatise of the diseases of Children. London, Stephens, 1653. (Fund for rare books.)

Perry, Charles. View of the Levant, particularly of Constantinople, Syria, Egypt, and Greece. London, Woodward, 1743. (By purchase.)

de Vigo, Joannes. Most excellent works of chirurgerye made and set forth by maister John Vigon. (London), Whytchurch, 1543. (Fund for rare books.)

Vesalius, Andreas. De humani corporis fabrica librorum epitome. Basileae, Oporini, 1543. This work is extremely rare. It was issued

unbound, and, in consequence, perfect copies are seldom found. The present copy lacks three leaves—C, G, and L. (Presented by Dr. Harvey Cushing.)

Manuscript

Finch, Heneage (Earl of Nottingham). Commonplace book. (London), 1647. An extremely precious book. Contains some odd notes and memoranda by Finch and others; but its great value consists in having two pages, 582 and 583, the contents of which are written and signed by William Harvey for his nephew and patient Heneage Finch, about 1647. Nowhere, it is said, outside of the British Museum, can so much of Harvey's writing be found. (Bequeathed by Dr. S. Weir Mitchell.)

Other Interesting Accessions

American Medical Association. Four badges. (Presented by Mr. Charles Perry Fisher.)

Barton, John Rhea. Marble bust by P. Romanelli. (Presented by Mrs. John Astor and Mrs. Francis C. Lawrance.

Harvey, William. Cup and saucer with the Harvey arms, from the Harvey mansion, Essex, England. (Presented by Dr. John K. Mitchell.)

International Medical Congress. Badge of the Ninth Meeting. (Presented by Mr. Charles Perry Fisher.)

Storer, Horatio R. Bronze medal designed by R. Tait McKenzie, M.D. (Presented by Dr. Henry Barton Jacobs.)

Turner's Lane Hospital, Philadelphia. Four photographs, framed. (Presented by Dr. John K. Mitchell.)

Yale University Medical School. Badge with bronze medal, commemorating the centennial of its foundation. (Presented by Dr. William W. Keen.)

Portraits

Harvey, William. Copy of original portrait. (Bequeathed by Dr. S. Weir Mitchell.)

Hunter, John. Copy of original portrait. (Bequeathed by Dr. S. Weir Mitchell.)

McClellan, George. Portrait in oils by Julian Story. (Presented by Mrs. George McClellan.

Morton, Thomas G. Portrait in oils by H. H. Breckinridge. (Presented by Mr. Arthur V. Morton.)

Osler, Sir William, Bart. A signed crayon sketch by Sargent. (Presented by Lady Osler.)

The Committee on the Mütter Museum has submitted a very favorable report. There has been an increased use of the collections by Fellows of the College and others for the purpose of investigation and teaching. Comprehensive plans for the better utilization of the space and display of the exhibits are being gradually carried into effect. The Lecturer this year was Dr. Albert H. Albee, of New York City, who selected for his subject, "The Fundamental Principles Involved in the Use of Bone Graft in Surgery."

The Hall Committee has administered its arduous and responsible duties with economy and efficiency. The garden planted to commemorate Wharton Sinkler has been the source of great pleasure to the Fellows and the general public, and the appearance of the Hall and its various departments has been highly satisfactory.

The Committee on the Directory for Nurses has had another year of social service in which the people, the nurses themselves, and the physicians of the city and the surrounding parts have been alike beneficiaries. The usefulness of this work is largely dependent upon the influence and support of the medical profession and I earnestly bespeak for it the increased interest of the Fellows of the College.

The Committee on Finance, of which the Treasurer is an active member, has given the most careful attention to the investments of the College and its receipts and expenditures. The condition of the properties has been systematically examined, necessary changes in insurance have been made and the financial interests closely watched in every respect. The cost of carrying on the affairs of the College has considerably increased in recent years. Fortunately the revenues have also increased and the deficit usual at the close of the year is not great. The time is not distant when we may hope that the distribution to the residuary legatees of the estate of Dr. Duhring will take place. This fund will greatly increase the income of the Library and correspondingly diminish the annual appropriation made by the College for library purposes. We will then be able to set aside from year to year a larger pro-

portion of our income to capital account, and thus guard against financial difficulties. In this connection I may remind you that changes may occur in the matter of the taxation of properties in this city occupied by ecclesiastical, charitable, and educational organizations, or that the tenant of the old College building might under certain circumstances fail to renew the lease. Other possibilities will suggest themselves. It therefore behooves us regularly to live within our income. A friend of the College, whose abundant generosity enabled us to finally discharge the balance of indebtedness incurred by the Building Committee, accompanied his gift with a brief but significant word of advice—"Now you are out of debt, keep out." At any rate, we must exercise that reasonable prudence in the matter of our expenses which is becoming to an institution of learning.

The Committee on Scientific Business has with the help and coöperation of the Fellows of the College experienced little difficulty in securing a series of papers of more than usual interest and value for the meetings of the year. To this phase of our work, I called your attention earlier in my address. The committee reports that it incurred no expense during the year.

The Committee on Public Health and Preventive Medicine has again justified its recent addition to the list of our Committees by its activity in its field of work, its coöperation with the Director of Public Health and Charities and its interest in arranging "A Symposium on Municipal Hygiene" for our meeting of May 6, 1914.

The thanks and high appreciation of the College are due to all these Committees and their Chairmen for the discharge of duties that have added another useful year to the history of our College, and I take great pleasure in expressing our recognition of their services and our sense of obligation to them.

At the December meeting it was announced that a Supplemental Deed of Trust had been executed by which the "Nathan Lewis Hatfield Prize for Original Research in Medicine" will be known hereafter as the "Nathan Lewis Hatfield Prize and Lectureship Fund"—one or more lectures to be given annually upon such

subjects and at such times as shall be approved by the Trustees, in addition to the awarding of a Prize for Original Research in Medicine.

At the January meeting the President announced the gift of fifteen thousand dollars presented by Miss Fannie S. Magee, Miss Anna J. Magee, and Mr. James R. Magee in memory of their brother Horace Magee, with the request that this sum be properly invested and known as the "Horace Magee Memorial Book Fund," and the thanks of the College were tendered to the donors.

At the same meeting the President announced that he had received from Dr. S. Weir Mitchell, as Custodian of the Rush Watch, May 26, 1913, after the death of Dr. Billings, a sealed letter to be opened on Dr. Mitchell's death, appointing a new Custodian. The President then opened the letter, which contained the name of Dr. Simon Flexner, of the Rockefeller Institute of New York, as the life Custodian of the relic. Dr. Flexner has since forwarded to the College a sealed letter containing the nomination of his successor in this custodianship.

At the April meeting action was taken by the College in regard to an amendment contained in the Army Appropriation Bill, transferring the Library of the Surgeon-General's Office to the Congressional Library, a measure involving the discontinuance of the publication of the "Index Catalogue" and the "Index Medicus." The College passed a resolution, drawn up by the Honorary Librarian, setting forth the irreparable injury to medical research such an enactment would cause. It is satisfactory to know that the amendment in question failed to pass.

At the October meeting the President announced the gift of five thousand dollars from Mrs. Henrietta B. Wyeth, in memory of her late husband, Francis Houston Wyeth, this sum to be invested and known as the "Francis Houston Wyeth Fund"—the income to be used in defraying the expenses of the publication of the TRANSACTIONS and such other publications as the College may determine.

At the same meeting the Treasurer announced the receipt of one thousand dollars from Dr. J. Ewing Mears on account of the "J. Ewing Mears Library Fund."

At the November meeting the Treasurer announced the receipt of an additional sum of one thousand dollars from Dr. Mears, thus completing his contribution of five thousand dollars for the "J. Ewing Mears Library Fund."

The Alvarenga Prize for the year 1914 was awarded to Dr. H. B. Sheffield, of New York City, for his essay entitled "Idiocy and Allied Mental Deficiencies in Infancy and Early Childhood."

Dr. Thomas R. Neilson, who served the College as Secretary faithfully and with great efficiency from 1896 until May 6, 1914, was obliged during the year by increasing professional duties to resign his office. It is as difficult to realize the amount of work such a service demanded as it is to appreciate how conscientiously it was performed. You will join with me in the expression of the most sincere thanks of the College to a most valued officer.

In the course of the year just ended the College has lost by death six Fellows:

Dr. S. Weir Mitchell, elected a Fellow in 1856, died on January 4, 1914. The most accomplished and versatile physician of our times, Dr. Mitchell's life was one of uninterrupted activity from early manhood until the end. His scientific and intellectual gifts and his untiring energy won the fullest recognition of institutions of learning here and abroad; his services to humanity, the gratitude of a world. To this College he was in the highest sense an eminent benefactor. Naturally a leader, he led us in the right way. His scientific work was clean cut, original and suggestive; his interest in the books unflagging; his knowledge of men at all times most helpful. His hand was always open. He created the Mitchell Book Fund, the Mitchell Entertainment Fund; he made this building possible. He was in the highest human sense a great physician.

Dr. Morris Longstreth, elected a Fellow in 1877, died at Barcelona, Spain, on September 19, 1914. At one time attending physician to the Pennsylvania Hospital, he developed an especial interest in the therapeutic management of chronic diseases and established a broad reputation as a practitioner. His frequent and prolonged absences from Philadelphia interfered much with

his interests here. Nevertheless, he bequeathed one-half of his residuary estate to this College, the other half going to Harvard University, of which he was an alumnus.

Dr. Joseph Scribner Gibb, elected a Fellow in 1892, died on November 7, 1914. Bringing to the specialty in medicine, to which he devoted himself, talents of a very high order, he early achieved an enviable reputation and was appointed Professor of Diseases of the Nose and Throat in the Philadelphia Polyclinic and Surgeon to the Ear, Nose, and Throat Department of the Episcopal Hospital.

Dr. William R. Bullock, elected in 1851, and the oldest living Fellow, died on November 18, 1914. An alumnus of Harvard University and a graduate of the School of Medicine of the University of Pennsylvania, he devoted a long life to the successful practise of his profession in Wilmington, Delaware. Of gentle manners and fine literary tastes, he found congenial occupation for his leisure hours in connection with the management of the Wilmington Institute and Library and the Board of Education of which he was for a long time president. The later years of his life were spent in retirement.

Dr. Sherborne W. Dougherty, elected a Fellow in 1902, died on November 23, 1914. An alumnus of the University of Pennsylvania, of the Class of 1889, and a graduate of the Medical School of 1892, Dr. Dougherty early manifested unusual zeal and devotion to his profession. He was resident physician in the German Hospital; later, Physician to its Dispensary and Assistant Physician to the Methodist Hospital, positions which he held until the time of his death. To a high order of ability as a practitioner he added engaging manners and broad intelligence, and will be greatly missed by those who depended upon his skill.

Dr. Charles H. Reed, elected a Fellow in 1887, died on November 23, 1914. Gifted with fine musical abilities, he early devoted himself to that art as an amateur, to the sacrifice of opportunities which would have made him a useful and successful physician. Notwithstanding this fact, he continued to maintain an interest in this College until his death.

The death of three Associate Fellows was reported during the year: Dr. Hughlings Jackson died on October 7, 1911. Dr. Oliver F. Wadsworth died on November 29, 1911. Neither of these has been previously announced. Dr. William Pye Smith on May 23, 1914.

Two Fellows have resigned. Thirteen new Fellows have been elected, making a gain of five in the Active Fellowship.

The roll of the College on December 1, 1914 shows:

Fellows		472
Associate Fellows:		
American	21	
Foreign	15	
	—	36
Corresponding Members		2
		510

I cannot close this address without alluding to important changes in the By-Laws which were passed at the meeting of December, 1914. The first of these revisions provides for a very moderate reduction in the entrance fee and the annual dues. It was the thought of the Fellow who suggested this change that it would be acceptable to a number of the younger Fellows, that it would bring into the College some of the junior teachers and salaried workers who are hesitating at present to come and that it would be more in accordance with the custom of scientific organizations, without impairing our power for usefulness.

The other relates to the Weir Mitchell Lectureship. That Committee is replaced by the Committee on the Mitchell Oration. It shall be the duty of this Committee, appointed by the President every third year, to designate and appoint, subject to the approval of the College, a Fellow of the College or a distinguished physician not a Fellow, to deliver the Weir Mitchell Oration at a Special Meeting to be held in the autumn of the second year after the appointment of the Committee.

This triennial oration shall have for its subject the life and work of Weir Mitchell in their various aspects, or the relation of the physician to public life, or the physician in science and letters, or broad considerations of psychiatry and neurology, or surgery and military surgery in relation to morbid conditions and wounds and injuries of the brain and nervous system, or the subject of scientific research, or medical books and libraries, or medical history and biography, and shall be, so far as possible, of general as well as professional interest.

By the recurrence of this formal event the memory of the greatest friend the College has had will be kept constantly renewed, the example of the most distinguished physician of our times recalled to the Fellows of the future, and the College, by doing honor to one who greatly honored it, will do honor to itself.

GASTRIC ULCER[1]

By JOHN B. DEAVER, M.D.

I HAVE thought it of sufficient interest to bring before the College certain questions relative to the treatment of gastric ulcer which have interested me very much, and which I have worked out to my own satisfaction along lines not universally endorsed perhaps by surgeons doing this work, but which I feel sure will prove to be the solution of certain vexing problems.

The experience of the last few years of activity in gastric surgery has shown both brilliant successes and dismal failures. It has shown that no one operation will fit all cases, that variations in situation, chronicity, and complications demand different methods of treatment, until finally, by the slow evolution of clinical experience and observation, we are in a position to draw some conclusions as to the principles which should underlie the surgical treatment of gastric ulcer.

Speaking of gastric ulcer in general, we must all agree that the treatment is aided by understanding both the predisposing and provocative causes which are responsible for the condition. Greater knowledge along the latter lines enables us so to base our treatment as to attack the root of the evil. Direct traumatism, nervous and vascular conditions aided and abetted by the digestive and erosive action of the gastric juice, particularly when over-acid, have been the basis of the most advocated theories of the cause of this special form of ulcer. None of these explanations has stood the test of clinical parallel or sufficed to explain the revelations which have been brought about through the medium of the aseptic scalpel.

[1] Read January 6, 1915.

That peptic ulcers are at the outset due to some form of toxemia or infection there is no doubt in my mind. The clinical arguments in favor of toxemia and infection being the causative factors are devious, and may not in themselves be conclusive, yet, as is often the case with such beliefs, evidence of a more satisfactory nature has appeared after a time. We know that experimentally (Turk) gastric ulcer has been produced by intravenous injection of the colon bacillus. Recently, Rosenow has demonstrated that certain strains of the streptococcus when inoculated into the blood of experimental animals produce ulcers of the stomach and duodenum with great uniformity. Gundermann has produced both acute and chronic ulcers of the stomach by ligation of the left hepatic branch of the portal vein, concluding that an hepatic toxemia is the cause of the ulceration. Experimental evidence, therefore, is not lacking as to the role that toxemia, whether metabolic or bacterial in origin, may play in causing gastric ulcer.

Appendicitis is by far the most common intra-abdominal disease. If we admit that appendicitis is always caused by infection, and that it is the most common intra-abdominal disease, we must also admit that the appendix, therefore, is the most common avenue by way of which infection reaches the abdominal circulation, be it through the blood or lymphatic current. Granting this is true, we have the keystone of the arch of the knowledge of intra-abdominal diseases which always are the result of an infection. I believe the appendix is responsible for liberating the infection, which in turn causes gastric as well as duodenal ulcer and other forms of upper abdominal disease in an overwhelming majority of instances.

In my clinics at the German Hospital I have observed the almost constant association of chronic appendicitis and gall-bladder disease with duodenal and gastric ulcer. Paterson also calls attention to this point. Graham, in the Mayo statistics, gives 23 per cent. of duodenal ulcers and 20 per cent. of gastric ulcer coexistent with disease of the appendix and gall-bladder. The focus of infection need not necessarily be the abdomen, though it seems that it is here the association is more evident.

That infection from the mouth, as occasioned by pyorrhea,

for example, may be the exciting factor in causing gastric ulcer is true perhaps in a small percentage of cases. Doubtless there are many portals of entry for infection, but it is sufficient to say that we are warranted in assuming that chronic or acute infections with the toxemia or bacteremia consequent thereon are capable of producing and do, under clinical conditions, produce gastric and duodenal ulcerations. Furthermore, the common association of chronic disease of the appendix with gastric and duodenal ulceration is significant of a causal relation between the two through the medium of toxic products and infection liberated from the appendix.

We are concerned equally as much with the factors that keep the ulcer from healing as with those that give rise to it. Among these are the conditions of the general health, the continuance of exciting causes in the muscular activity of the stomach, the action of the gastric juice upon eroded surface, and infection that implants itself upon the bed of the ulcer. That there is a strong natural tendency for simple gastric ulcers to heal there can be no doubt, as there is abundant evidence of such healing in the human. Experimental ulcers usually close rapidly.

Well-directed medical treatment will succeed in healing most acute ulcers and a fair percentage of those on their way to chronicity. In the absence of severe complications, medical treatment should always be given a fair trial before resorting to surgery.

Ambulatory treatment will rarely be successful except in the simple form of ulcer. If anything is to be expected of medical treatment in the chronic types of ulcer it must be radical, demanding four to eight weeks' rest in bed and most careful feeding. The entire remission of all symptoms, which is a characteristic of ulcer, has been productive of much misunderstanding and harm. It must not be forgotten that ulcer is productive of symptoms, as a rule, only when it is in an inflamed and active state. When the bed of the ulcer is covered with insensitive granulation tissue, and its walls are not inflamed, pain and distress are abolished, and unless adhesions or cicatricial deformity are present, the patient feels quite well and the incautious physician may be led to believe

that the ulcer is healed. It is not difficult to lull an inflamed ulcer into quiescence, but it takes time, patience, care, and coöperation on the part of the patient to await the time necessary to reinvest the ulcer with epithelium. In this quiescent stage many a patient has been placed asleep in the eternal rest of the grave.

The explanation of recurrent attacks extending over many years is to be found in the fact that at no time was the ulcer healed. Circumstances render it impossible in many instances for the patient to submit to the rigorous regimen necessary for cure, and in many other cases it is equally impossible to secure the coöperation of the patient in the tedious process. Attempts at healing by medical treatment with the best means available is justified in all except those cases complicated by perforation, recurrent hemorrhage of sufficient moment to cause material drain upon the patient's health, or in the presence of persistent indigestion that does not yield after a fair trial of medical treatment, by which I do not mean indefinite temporizing. We must not forget the marked tendency of cancer to develop on a chronic ulcer base, and all such cases are properly to be rated as the most disastrous medical failures.

Admitting the conditions just stated to be the correct clinical indications for operation, we come to the consideration of surgical procedures, about which there is not as yet unanimity.

There is a difference of opinion among surgeons as to the correct procedure in perforation. Some contend that only the perforation should be closed. Others believe that a simultaneous gastro-enterostomy not only aids permanent cure, but also increases the chances of recovery in acute perforative conditions. While it may appear on the surface that simple closure of the ulcer would suffice for the immediate emergency, and that the less surgery, the greater likelihood of recovery, nevertheless it is my belief that a primary gastro-enterostomy is far more likely to be followed by immediate recovery, and certainly the prospects of future relief are much improved. The mortality of those who combine gastro-enterostomy with closure of the ulcer is superior to that of those who practise only closure. I have reported thirty cases of acute perforation of gastric and duodenal ulcer in which gastro-enterostomy was done

as a primary procedure, with one death. Since then I have had three additional cases, with recovery.

Hemorrhage, whether massive, recurrent, or occult, will furnish different indications according to the lesion believed to be present, its duration, the amount and seriousness of the loss of blood. Profuse gastric hemorrhage in the young without previous symptoms of ulcer may be due to mucous erosions or hemorrhagic gastritis. The cause of these so-called Dieulafoy's ulcers may not be clearly understood, yet clinical experience shows that they are not ordinarily fatal, tend to clear up spontaneously, and often are followed by no sequel of any kind. Gastro-enterostomy has been advocated for these conditions, but the evidence, in my opinion, does not warrant its use in every case. On the other hand, massive hemorrhage from erosion of the base of a chronic ulcer is a dangerous condition and urgently calls for intervention. At the same time it is not wise to operate upon a patient in an exsanguinated state. The first hemorrhage rarely kills, and with proper treatment some reaction may be expected. On the other hand, reaction with restored blood-pressure is apt to excite fresh hemorrhage, which is more likely to be fatal than the first. It becomes a question of nice surgical judgment, therefore, to decide when to operate. I have regretted my decision in both directions, and do not feel able to advise in any other than the most general terms. It is too hazardous to wait for the reformation of blood to take the place of that which was lost, as that is a matter of some days and even weeks. This being the case, it seems wise to wait only for the subsidence of shock, the refilling of the bloodvessels by the body fluids, and by water administered and the restoration of the blood-pressure to approximately normal level. Direct transfusion of blood will occasionally have a field here.

In these cases one's difficulties are not over with the selection of the best time for operation. The location of the actual erosion in the vessel is a matter of the greatest difficulty. It is difficult to determine which artery is affected. Direct ligation is therefore theoretically desirable, but practically well-nigh impossible. Complete excision of the ulcer is almost invariably too much of an

operation for these patients to stand. Simple gastro-enterostomy may be helpful but does not provide absolute security against recurrence of bleeding.

A plan which I have followed successfully appeals to me as sufficiently radical. After opening the abdomen and locating the ulcer the stomach should be opened and the base of the ulcer inspected. If the vessel is seen it should be ligated directly by transfixion. If, as is more commonly the case, no erosion or vessel is seen, a stitch of catgut should be whipped around the base as

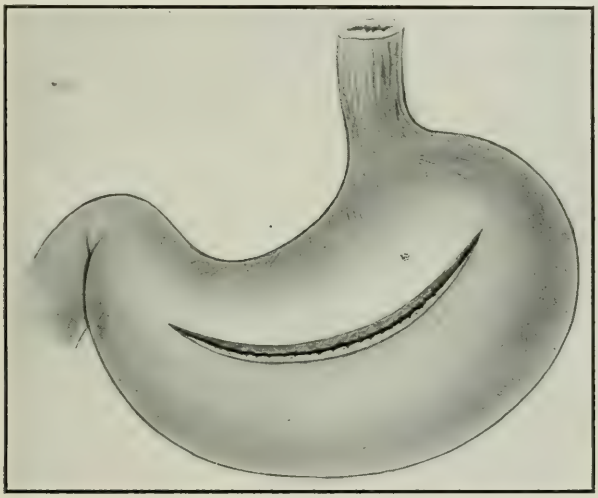


Fig. 1.—Incision through anterior wall of stomach.

well as the edges of the ulcer, with the object of occluding the vessel supplying it. The stomach may then be closed and gastro-enterostomy quickly performed. I liken this procedure to hysterotomy, of which I am a strong advocate.

Further, it is my practise, where the ulcer cannot be located by inspection and careful examination of the exterior of the stomach, to open widely the stomach through the anterior wall and inspect its interior throughout, which can be done satisfactorily, as I have frequently demonstrated. The latter treatment, as a matter of course, applies to chronic ulcer more than to acute ulcer. That

the danger in opening the stomach in chronic ulcer cannot be great is proved, moreover, by the fact that I have operated upon thirty-three cases of acute perforation of the stomach and duodenum with but one death. In these cases there is much more soiling of

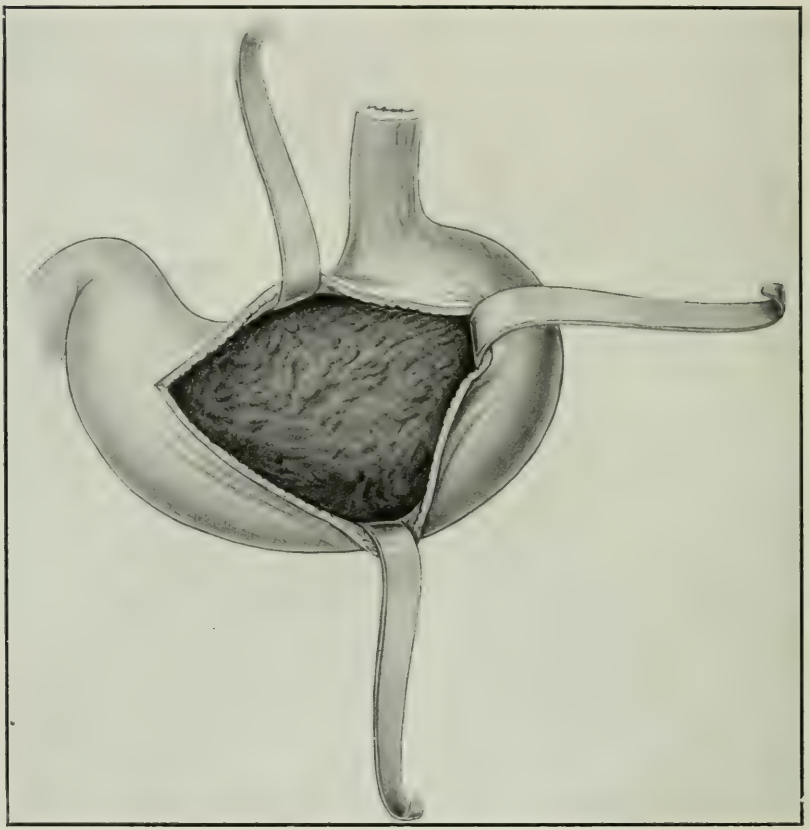


Fig. 2.—Margins of incision retracted, showing interior of stomach.

the peritoneum by gastric contents than could result from a properly performed gastrotomy.

The degree of fibrosis in the wall around a gastric ulcer varies. It may be so slight that the ulcer is not easily felt; this is particularly so when it is situated close to the pylorus (pyloric ring). This is

one of the reasons why I open the stomach in cases where I cannot satisfy myself as to the presence of a lesion. The area of open ulceration is not necessarily related to the extent of sclerosis of the wall of the stomach. The physical character of an ulcer has an important bearing on the question of excision. Ulcers on the posterior wall of the stomach are more frequently adherent to surrounding structures than those on the anterior wall.

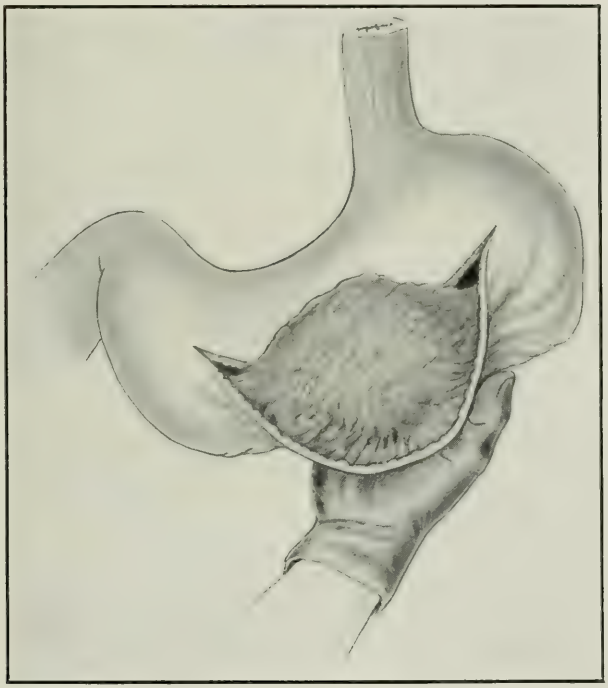


FIG. 3.—Wall of stomach everted through gastrotomy incision.

The effect of gastro-enterostomy when ulcers are some distance from the pylorus is often disappointing. Gastroduodenostomy has an important field in surgery of ulcers close to the pylorus. The latter operation positively excludes pyloric spasm and retention, two most important phenomena in gastric ulcer. Excision is influenced by the site of the ulcer, adhesions, and the general condition of the patient.

Smaller hemorrhages, if persistent, also strongly indicate surgical measures, since we cannot determine just what artery is being attacked; and even if it is not a precursor of serious hemorrhage the patient's vitality is much affected by constant loss of small quantities of blood.

Chronic ulcers situated along the lesser curvature of the stomach I always excise. This is accomplished by first opening the lesser peritoneal cavity through the upper layer of the gastrohepatic

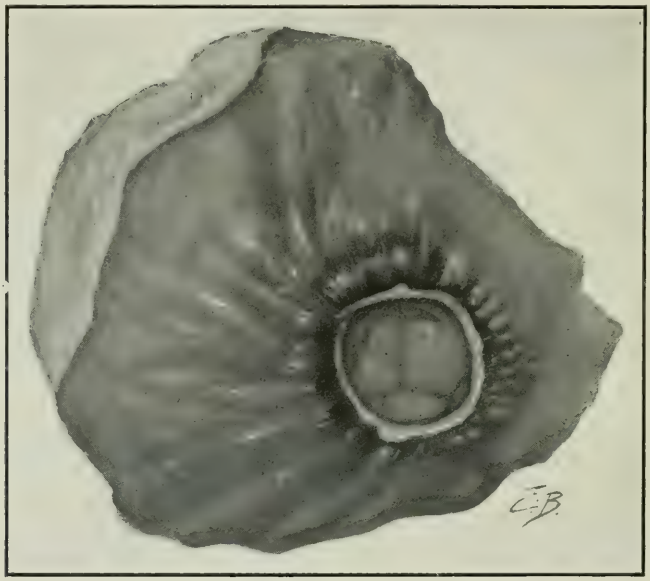


Fig. 4.—Ulcer, posterior wall.

omentum, tying the coronary artery to the left and the pyloric artery to the right, then opening directly through the anterior wall of the stomach, exposing the ulcer, cutting it out with scissors, closing the stomach, and finishing the operation by posterior gastro-enterostomy and plication of the duodenum. I have done several of these operations and up to the present without a fatality.

I have recently performed a transduodenal excision of an ulcer in the internal posterior wall of the duodenum in its second portion. The crater-like fibrosis around the excavation of the ulcer was

felt through the anterior wall of the duodenum, where it lay on the head of the pancreas which at that point showed induration and evidence of chronic inflammation. Through a longitudinal incision in the duodenum the ulcer was exposed and was then excised with the scissors and knife. The defect in the posterior wall was brought together with stitches of chromic catgut and the opening in the anterior wall closed with chromic gut and linen thread. A posterior gastro-enterostomy was made and the patient recovered. This I believe is the first instance of such an operation for duodenal

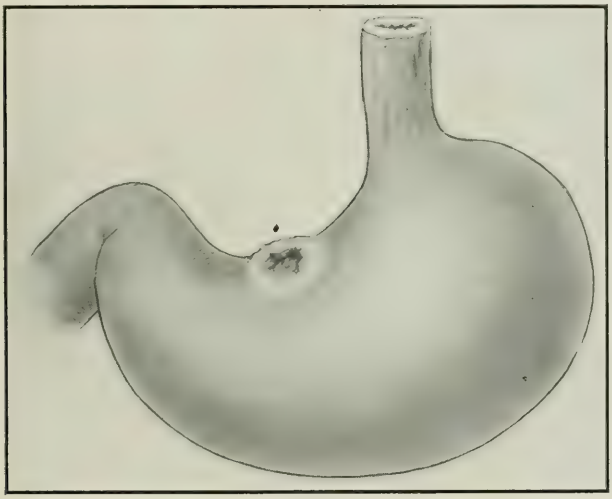


FIG. 5.—Ulcer, lesser curvature of stomach.

ulcer. It is applicable only to ulcers similarly situated which have not eroded completely through the wall into the adjacent tissues.

This case shows what may be done early in the history of gastric or duodenal ulcer. The later the case, the more widespread is the ulcer and its consequences, the more difficult is the surgery and the less satisfactory the results.

Ulcers of the posterior wall of the stomach distant to the lesser curvature I expose by opening the stomach and the lesser peritoneal cavity which affords oportunity to deal with the ulcerated area with the least difficulty, following the latter with a posterior gastro-

enterostomy. In ulcer of the pyloric portion of the stomach, unless very small and not indurated, I perform pylorectomy.

If perforation or conspicuous bleeding are absent, at what point does a gastric ulcer cease to be a medical condition? Clearly, it seems to me, when it is seen that such medical treatment as can be employed fails in a reasonable time to cure the ulcer. *Cure* should be sharply distinguished from *remission* or improvement of symptoms. Recurring ulcer symptoms mean only one thing, failure of cure, and to incur the risk of the grave complications which are likely to follow chronic relapsing ulcer is an unjustifiable assumption

Fig. 6.—Ulcer, internal posterior wall of duodenum.

of responsibility. We must not stop short of surgery if the ulcer is refractory to other methods. One relapse after thorough treatment, two or at the most three relapses after treatment imperfectly carried out should convince one that chronic ulcer of a refractory type is present.

The question of the proper surgical treatment of a gastric ulcer can be decided only after the abdomen has been opened and the condition present thoroughly explored, which often means that the stomach must be opened widely to make the exploration thorough, as I have referred to above. Complete excision of the ulcer may be spoken of as the ideal treatment, but, like ligating an eroded vessel

in an ulcer bed, or many other measures theoretically ideal, it can seldom be accomplished. Localized saddle ulcer on the lesser curvature, ulcers strictly limited to the pylorus or small punched-out ulcers elsewhere in the wall, are those which are best adapted to excision. Given a patient in good general condition, and an ulcer that can be so removed that subsequent closure can be made without undue distortion of the stomach, and without tension and

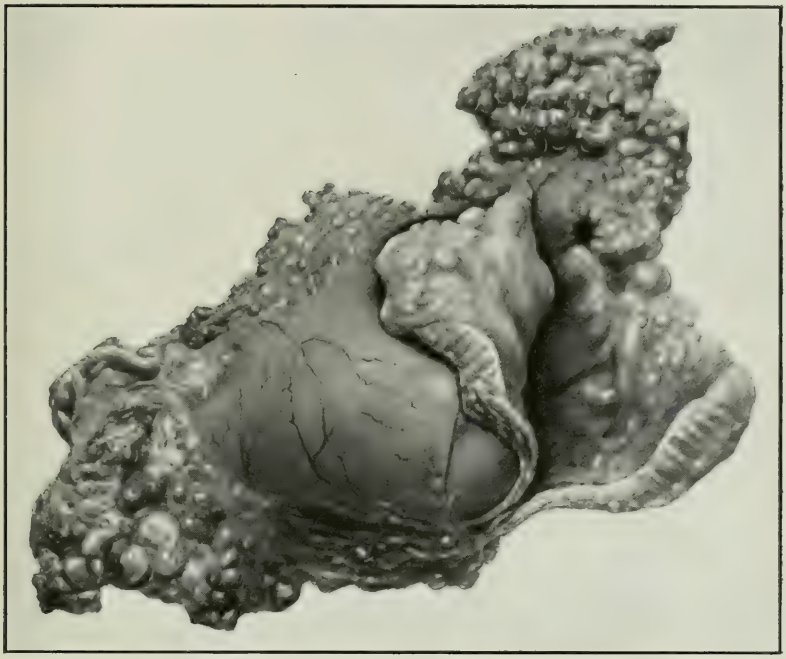


Fig. 7.—Ulcer, lesser curvature.

danger of leakage, excision is the method of choice. If such an ulcer be unusually hard and suspicious of malignant degeneration, there is the greatest need for excision, or better still, subtotal gastrectomy. If excision has been done, it is best to make a gastro-enterostomy even though the pylorus has not been encroached upon. A method of removing the ulcer completely is the so-called exclusion, which consists in placing occluding ligatures through all

the thickness of the stomach wall, encircling the ulcer completely, and cutting off its blood supply so that it separates as a slough by ulceration into the interior of the stomach. The occluding ligatures having been tied the walls of the stomach immediately adjacent are apposed. This method should be ideal in bleeding ulcers, as hemostasis is at once affected by the ligatures. In many situations,

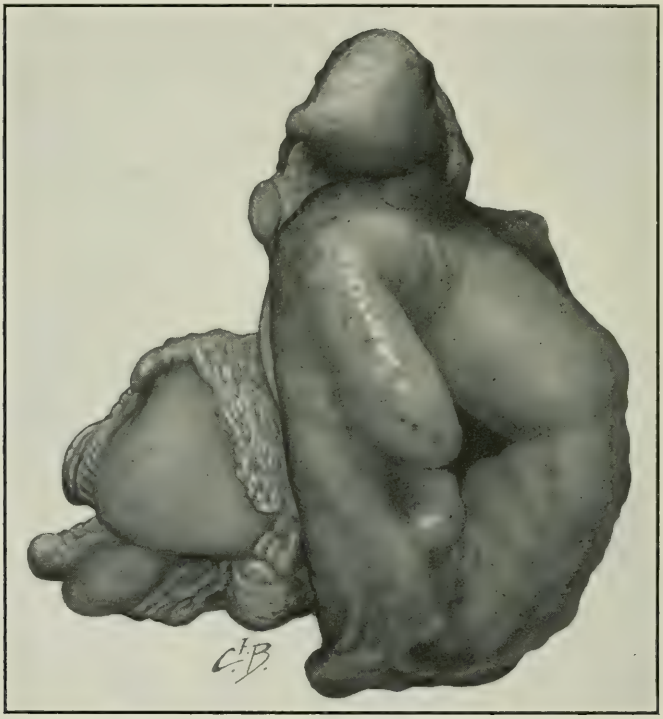


Fig. 8.—Ulcer, pyloric end of stomach.

however, it is impossible to apply this variety of ligature, and I believe that this method is of little real utility. I have never done this operation.

Ulcers high up in the fundus of the stomach are the most difficult to treat. Gastro-enterostomy fails to effect a cure. Excision is usually impossible because of its difficulties and the great

operative hazard. These may be treated best in an indirect manner by jejunostomy, which gives absolute rest to the ulcerated surface and favors healing.

One of the most important points to be noted in connection with this subject is the fact that the sufferer from gastric ulcer does not belong to either the internist or the surgeon exclusively. The physician should make the first attempt at cure, and in the event of failure or sudden catastrophe the patient becomes surgical. If he can have his ulcer excised he may be through with his physician so far as this particular condition is concerned. If, as more often

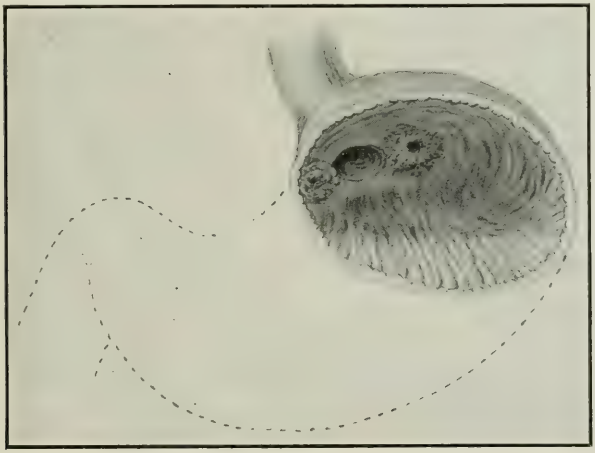


FIG. 9.—Ulcer at esophageal opening of stomach.

happens, the surgeon finds it impossible or unwarrantably dangerous to excise the ulcer, he employs an operation which depends for its efficacy chiefly upon rest for the affected area. The patient should then return to his physician, who will so direct his diet and mode of life as best to assist in this object. Right at this point many failures occur. Either the physician fails to appreciate the importance of careful supervision or the patient, completely relieved of his symptoms, believes that he is cured, and can indulge his appetite as freely as he wishes. This is particularly true of patients who have had more or less pyloric stenosis. Their relief is so great

and their hunger in their half-starved condition is so compelling, that if not restrained they will go to extremes in eating that no sound man could endure. In this case the ulcer may be deprived of its rest and protection and fails to heal, or in still other cases additional ulcers form elsewhere. A goodly percentage of recurrences are due to such failure of the patient or his physician to carry to completion the work only begun by the surgeon.

Finally, in view of the fact that prevention is greater than cure, and particularly because it is seen from this brief review of certain mooted points in the surgical treatment that cure is difficult and perhaps impossible, I would urge the propriety of acting on a well-reasoned suspicion that a small inhabitant of the right iliac fossa is responsible for much of the serious diseases of the upper abdomen. In other words, search diligently for evidences of chronic disease of the appendix in all digestive disorders and treat it to a drumhead court martial at the first sign of insubordination.

DISCUSSION

Dr. John H. Gibbon: I think every surgeon can subscribe to practically everything Dr. Deaver has said. I wish I could feel quite as enthusiastic about the results obtained in perforation as Dr. Deaver. My experience is not in any sense comparable to his. I have operated upon twenty cases of perforation with a much higher mortality than Dr. Deaver's, and much nearer that usually accorded this operation. However, I have lost only one patient operated upon within the first twenty-four hours following perforation. From what Dr. Deaver has said I judge his cases were mostly, if not entirely, early ones. I think some of these perforations are overlooked and the cases looked upon as cases of general peritonitis and not operated upon because of the advanced stage. If we could tell absolutely that there was not a perforating ulcer, this non-operative plan might be followed. I cannot agree with Dr. Deaver as to the value of the *x*-rays. I would place my reliance upon (1) history, (2) *x*-ray study, especially with the fluoroscope, and (3) gastric analysis. W. J. Mayo places the *x*-ray study first, history second, and gastric analysis third. The röntgenologist has become so expert

now, especially with the fluoroscope, that I must say I think his help is invaluable in the diagnosis of this condition. Dr. Deaver and I disagree concerning gastro-enterostomy in the presence of perforation. In certain classes of cases, of course, I should do the operation, in those cases in which there is marked obstruction of the pylorus from the infolding of the ulcer and in which it is possible to operate early. With the stitches placed deeply around the circumference of the ulcer, healing occurs in the majority of cases provided the patient is starved a sufficient length of time after the operation. There is certainly no objection to doing the ideal operation except in cases in which much time has elapsed between the time of perforation and that of the operation.

Dr. John B. Roberts: The point made by Dr. Deaver concerning the etiology of gastric and duodenal ulcers has interested me very much. My attention was called to this matter years ago because I lost a patient upon whom I had done suprapubic cystotomy for stone, with sudden collapse ten days after operation. Autopsy showed a large perforated gastric ulcer, of which I had no knowledge, and which came, probably, as the result of the cystotomy. That was a good many years ago. A few years ago I had another case, ulcer in the duodenum, which followed rupture of the bladder—traumatic rupture of the bladder. In looking up the subject I was surprised at the large number of cases on record. There were at least a dozen cases of ulcer of the stomach and duodenum the result either of disease of the abdomen or of operative attacks upon the abdomen. I think Dr. Deaver is right in respect to the probable causative relation between suppurative disease of the appendix or of the gall-bladder, and these gastro-duodenal ulcers. His paper is to my mind a very important contribution to what I would call clinical pathology.

Dr. James Tyson: In my experience the diagnosis of gastric ulcer when not checked off either by operation or autopsy has not been very satisfactory. On the other hand, ulcers are sometimes found in the stomach at autopsy when no symptoms have been present before death. Only a few of the digestive symptoms have a distinctive value. Perhaps the most valuable one is copious hemorrhage. Small hemorrhages occur with cancer of the stomach but rarely large hemorrhage such as that which causes a patient's death. The value of gastric analysis never seemed to me to be very great, and I would put it third, rather than first in the order of value, making tumor second. We used to take a great deal of trouble to distinguish between gastric ulcer and gastric cancer. It does not make much difference at the present day, because operative treatment is the treatment to which we come sooner or later and the sooner the better. I believe that a large number of the cases which used to come to hospitals in the past and were diagnosed ulcer were not ulcer but simple chronic

gastric catarrh. Not more than one-third of gastric ulcer diagnosed by the methods of the day were really gastric ulcer. The presence of a palpable tumor is good evidence of gastric cancer, but a mistake is illustrated in the case of a man who came to me several years ago with history of recurring hemorrhage and evident tumor in the right hypochondrium. My colleague, Dr. William Pepper, 2d, then Professor of Medicine at the University made the diagnosis of gastric ulcer and the autopsy proved that he was right. I had made a diagnosis of gastric carcinoma because there was an evident tumor. The man bled to death twenty-four hours after admission to the hospital. There was found at autopsy a tremendous thickening of the pylorus, and down deep at the bottom of a clean-cut ulcer was a severed bloodvessel from which the man bled to death. I said to Dr. Pepper, "Why did you make that diagnosis which proved to be right when I was wrong?" He replied, "I had diagnosticated similar cases in another way so many times that I thought I would reverse it."

Dr. William E. Hughes: Dr. Jopson has reminded me of an exceedingly interesting case of duodenal or gastric ulcer in which the only symptom was hemorrhage, a quite profuse hemorrhage causing extreme anemia. Just before I saw him there was a less profuse hemorrhage causing only trifling anemia. There was no history of indigestion, but slight pain a few days before the last hemorrhage. The man died during the operation as the result of a very peculiar hernia through the diaphragm as the result of which practically all of the abdominal contents were in the chest. I want to put the case upon record because of its extreme oddity. There had been no symptoms at all with the exception of the hemorrhage, yet he carried his abdominal contents up toward the back of his neck somewhere. Dr. Gibbon has raised an interesting point in the diagnosis of peritonitis. I think that, as a rule, the diagnosis of perforation, either early or late, can be made with a fair degree of certainty by recognizing the presence in the abdominal cavity of free gas. Almost all the cases of perforating ulcer of the stomach and duodenum that I have seen have had this free gas in the peritoneal cavity within a few hours of perforation. The diagnosis, therefore, has been positive. In this condition of affairs it will persist throughout the subsequent peritonitis which occurs. I have seen very few cases of peritonitis in which there has been perforation without gas. I have seen a number of cases of perforating gastric ulcer and of duodenal ulcer and two cases of perforating typhoid ulcer of the intestines in which this gas has been present, and I regard it as a most important diagnostic feature.

Dr. John H. Jopson: I would like to say a few words in self-defence in regard to the patient referred to by Dr. Hughes, who died in the course of an operation for pyloric ulcer. The case had been seen by Dr. Hughes

in consultation with the physician, Dr. Ellis, and an immediate operation advised. The patient was in good condition before operation, but he took the anesthetic very badly. He became cyanotic and there was persistent rigidity of the abdominal muscles. When the abdomen was opened, the stomach was found enormously distended and there was a hard, circumscribed and stenosing ulcer of the first portion of the duodenum. It was proposed to do nothing but gastro-enterostomy. The first step after the enfolding of the pylorus with a couple of linen stitches, was to pick up the jejunum. Drawing out the transverse colon, I looked for the first portion of the small intestine below it. To my surprise, I did not find it in its usual site. I found the cecum and appendix high up under the mesocolon, near the median line, just below the stomach. Examination of the peritoneal cavity showed an entire absence of the jejunum and ileum excepting the terminal portion of the latter which could be traced for a few inches from the ileocecal valve where it blended with the posterior peritoneum. I thought of thoracic hernia and passed my hand above the stomach and liver and around the diaphragm on both sides, but felt no opening. I then opened the lesser peritoneal cavity through the transverse mesocolon and passed my hand into it, behind the stomach. This was followed by a profuse hemorrhage, both from the retrocolic vessels and from the perforation which this slight manipulation opened up in the posterior wall of the ulcer. From this opening a large amount of dark, liquid blood and solid food particles kept pouring in a flood, which could not be controlled, although repeated attempts were made to suture it. The patient's condition became desperate and he finally succumbed while we were suturing this large opening in the pylorus. A more thorough examination was then possible after the stomach had been lifted out of the abdomen, and we found a hernia of the entire small intestine excepting its beginning and termination, through an opening in the left side of the diaphragm, posterior to the stomach, into the thoracic cavity. Some of the coils of the intestine were adherent, so that they could not be pulled down into the abdomen. The condition was evidently congenital, as the edges of the opening were thick and rounded, and, in combination with the obstructing, bleeding, perforating ulcer, rendered the patient's condition incurable.

Dr. John B. Roberts: In connection with the case mentioned by Dr. Jopson I might say that I saw at the Mayo Clinic a case of congenital thoracic hernia. Dr. W. J. Mayo operated upon a young boy for curious vomiting attacks. To his surprise and the astonishment of all of us he found that the stomach was up in the left chest.

Dr. Deaver (closing): The majority of my cases were seen within twenty-four, some as late as thirty-six hours, and one seventy-two hours

after perforation. I therefore cannot agree with Dr. Gibbon that seeing the cases early explains entirely the low mortality. The colon bacillus was present in some but not in all of the cases. The chief object of gastro-enterostomy is to get these patients well more promptly and to keep them well. I would urge the occasional operator not to do a gastro-enterostomy but simply to close the ulcer. The little hospitals out in the country have not the equipment for this sort of work, at least, I don't think they have. I am not a strong advocate of the *x*-ray diagnosis in these patients and would prefer to open them up, when I can be sure. When the ulcer has brought about a pyloric stenosis, of course a diagnosis is easily made. Dr. Gibbon and I do not always agree, but we seem to agree tonight upon the etiology. Dr. Tyson rather hit the bull's eye when he said that exclusive of the postmortem slab and the operating slab he thought the diagnosis of gastric ulcer was not, as a rule, made. I have some faith in gastric analysis, but in these cases only when there is present a very high acidity. The case mentioned by Dr. Hughes and Dr. Jopson is very interesting. Had the man had his stomach opened up a few years before they would not have had this pathology to report.

MENDELIAN LAWS OF HEREDITY AND THEIR APPLICATION TO EUGENICS[1]

By ALFRED GORDON, M.D.

The conception of "evolution" in natural history became a solidly established acquisition with the advent of Darwin's *Origin of Species* in 1859. Following his genius an army of naturalists became convinced that the cause of variation of species lies exclusively in the operative influences of "natural selection." For a decade their view was the only one that held the largest majority of naturalists imperturbable. When, however, the problem of congenital diversity began to be studied more profoundly and the question of hereditary transmission commenced to arouse great difficulties for its solution, the significance of variation in individuals and species could no more be established on the basis of the old Darwinian conception. A new generation of evolutionists made its appearance. The experimental study of the species problem acquired a new orientation, and a complete revision of the former views became necessary.

The first serious attempt to disturb the Darwinian school was made by Weissman who insisted on actual proof of the fact claimed by Darwinians, viz., that acquired characters may be transmitted by parents to offspring.

Next in order of importance came the work of de Vries, who called attention to the great importance of the individual characteristics or "unit-characters" in the problem of hereditary transmission.

The principle of the unit-characters being at work in genetic processes constitutes the fundamental structure of Mendelian

[1] Read February 3, 1915.

laws of inheritance upon which modern evolutionary ideas may be solidly based. Let us therefore consider the essential features of Mendel's discoveries.

Mendel observed that in crossing plants possessing one strikingly different character or in mating animals differing in certain characteristics, the result will be that the first cross-bred plant or the first offspring animal exhibits the character of one parent to the exclusion of the opposite character. The character which is present he called "dominant" (D), the character which disappeared he called "recessive" (R). But while the latter is not seen in the immediate family, it is nevertheless present in a latent state and will reappear in the subsequent family or families.

This law of dominance was demonstrated by Mendel first on peas. By applying the pollen of a tall variety of the plant to the stigma of a very small variety he obtained seeds which grew all into tall plants. Tallness was therefore the dominant character, smallness—the recessive. The first generation or family is therefore composed of a pure character of one or of the other parent. The second and later generations on the contrary are characterized by polymorphism; each possesses characteristics resulting from combination of those of both parents. Mendel discovered that in spite of the polymorphous manifestations there is a certain regularity or law which can be traced in almost every case.

Pursuing the observations on peas it was noticed that in the second generation the products were of both kinds, tall as well as small; but three talls to one small, otherwise speaking, three dominants (D) to one recessive (R). In the third generation we find that the recessive give exclusively recessive, otherwise speaking, the small variety presented only small plants. But the dominants (tall ones) gave two kinds of offspring, viz., talls and mixed, the latter consisted again of three talls to one small. The same ratios may be observed in crossing yellow with green peas. Yellow color was found to be dominant over green. The first generation of seeds will all be yellow. Plants raised from this product presented both yellow and green seeds and in the ratio of 3 to 1.

In the next generation the green seed bore only green, while among the yellow, one out of three seeds produced only yellow and two produced green and yellow, three of the latter to each of the first, precisely what we have seen in the selection of the tall and small varieties. We therefore observe the proportion of three dominants to one recessive as being a constant characteristic feature.

Thus far two important conclusions may be drawn from Mendelian observations on plants. First, separation or dissociation of specific characters and their reappearance in the later formations of germs; this special feature is called *segregation*. Second, the constant ratio of three dominants to one recessive. The phenomenon of segregation is the most fundamental part of Mendelian laws of heredity. It emphasizes at once a regularity in transmission of hereditary features. It points out the direction in which certain units of characteristics may develop or else disappear.

Pursuing further our study of dominance or recessiveness of characters in plants, we find that the above enunciated laws are applicable to other characteristics besides those mentioned already. They are: shape of seeds (round or wrinkled), shape of pod, arrangement of flowers on the stem of the plant, branching, surface of the fruit, surface of foliage.

The principle of dominance and recessiveness which consists respectively of the presence or absence of a certain definite factor is equally applicable to animals. In normal conditions color inheritance has been well studied from this standpoint. Pigmentation has been shown to be dominant to absence of pigment. L. Cuénot[1] demonstrated that by crossing gray with white mice, one obtains in the second generation both kinds of mice and in the ratio of 3 grays to 1 white. The same may be observed by crossing gray rabbits with white ones. C. C. Hurst[2] studied the color inheritance in a variety of rabbits called "Dutch." In this animal the hind part is colored, gray or black; the front part is

[1] La loi de Mendel et l'hérédité de la pigmentation chez les souris, Compt. rend. Paris, T. 134, p. 779.

[2] Linn. Soc. Jour. Zoöl., 1905, xxix, 283.

white with the exception of a small portion on the ears and under the eyes which is gray or black. The crossing between a self-color and a Dutch gives in the first generation only self-color and in the second generation three self-color to one Dutch. This fact proves that the Dutch is a recessive.

The color of eyes presents interesting data from this standpoint. The pigmentation of the iris is the cause of differences in eye-color. Hurst has shown that brown eyes contain pigment, blue eyes are characterized by absence of pigment. The presence of brown pigment behaves as a dominant, while the absence of it, as a recessive. In albinos pigment is totally absent and the reason the eyes appear pink is because the light penetrates through a transparent iris. Albino behaves as a recessive to gray or black which are dominant. By crossing two pure albinos one obtains only albinos.

Albino should not be confused with whiteness; while in the first there is fundamental absence of pigment or rather absence of chromogenic substance, as Cuénot expresses himself, the latter may be caused by mere temporary suppression of the pigment-producing factors. A mating between such whites may result in colored offspring in the second generation a fact which is in accord with the principle of segregation described above. When an albino is crossed with a colored individual, the real absence of pigment in the first will be demonstrated if the particular color of the other individual happens to be recessive. In such cases the albino factor will be the dominant and will be manifested even in the first generation. The presence of the dominant albino element will bring breeds in which the color of the other mate will appear altered. Should the color of the other individual be dominant, we will find in the second generation 3 colored to 1 albino, the same constant ratio mentioned above. For example, on crossing a gray rabbit with an albino (gray being a dominant), the result will be: in the first generation gray; in the second generation 3 grays to 1 albino.

These several examples tend to prove that colors in animals as well as in plants may be altered by suitable matings. The latter

must follow the laws of dominance and recessiveness. This law has been observed in many other individual characteristics besides those already mentioned. A very curious and interesting phenomenon is the hereditary transmission influenced by sex. T. B. Wood,[1] for example, crossed horned (male and female) and hornless (male and female). In the first generation all the male elements had horns, the females had no horns. The horned character is dominant in males and recessive in females. The second generation presented all types, viz., horned and hornless males or females, and again in ratio of 3 to 1.

The influence of sex on inheritance can be also seen from the well-known condition called color-blindness. According to Bateson 4 per cent. of the male population in Europe and less than 0.5 per cent. of the female are color-blind. Color-blindness is a dominant characteristic in male and recessive in female. The same author speaks of the records of seven color-blind women whose seventeen sons were all color-blind. These facts point to a possibility that the female organism contains some element which inhibits or interferes with the effect of the dominant element.

This so-called sex-limited condition may be observed in other directions than color-blindness. Doncaster[2] for example has shown that the largest majority of tortoise-shell color of cats are females, while those of orange color are mostly males. Orange color is dominant in males. Tortoise-shell color is the result of combined influence of orange and black. The dominance is incomplete or imperfect in females, hence tortoise-shell color.

Extensive experimentation with regard to variations or limitations produced by sex, particularly the investigations conducted by Bateson and Punnett[3] in matings between certain fowls, such as Silkies with unpigmented Chanks, all tend to prove that sex is a problem which is governed by Mendelian laws. The fact that the above-mentioned interference with the operations of a

[1] Journal of Agricultural Science, vol. i, pt. 3, p. 364.
[2] Proceed. Cambr. Philosoph. Soc., 1904, xiii, pt. I, p. 35.
[3] Ibid., 1905, xiii, 165.

dominant factor occurs constantly in females, but not in males, leads one to conclude that femaleness itself is due to the presence of a dominant element.

The study of inheritance in man on Mendelian plan with regard to normal characteristics is still in its incipiency. Some advance has been made in the study of a few features, such as color of the eyes, the color and the general character of the hair, of stature. But unlike animals or plants in which, as it was mentioned above, the rules are simple, in man a great multiplicity and diversity of factors have an influence on the transmission of normal hereditary characteristics which therefore render the problem quite complex. However, carefully collected and recorded pedigrees are apt to bring light into this difficult subject. The studies of Hurst on eye-color, of Bell and Rizgoli on hair, of Mudge[1] on mulattoes, of Galtor on stature, prove that the proper effort in collecting data on normal characteristics through generations may render invaluable services in the study of Mendelian inheritance.

The study of abnormalities and of pathological conditions has been more fruitful. The reason of it undoubtedly lies in the facility with which striking dominant factors can be elicited and traced from generation to generation. Speaking generally it is established that abnormal features play the role of dominant in relation to normal features. Netleship[2] observed that various forms of cataract have played the role of dominant in his series of cases and he could trace them in several generations in which the pathological condition was transmitted chiefly through the affected members. He also reports a history of congenital night-blindness in nine consecutive generations[3] and all occurred through the affected persons. Night-blindness therefore behaved as a dominant factor. Various other eyes affections have been found to be dominants, such as glaucoma, coloboma, ptosis, and others.

Some skin or hair affections have also been traced as following

[1] Nature, November, 1907.
[2] Report of Royal Ophth. Hosp. in London, 1905, xvi, 1.
[3] Ibid., 1907, xxvii.

Mendelian laws of heredity. Gossage[1] speaks of keratosis palmaris and plantaris, xanthoma, telangiectasis, hypotrichosis congenita familiaris.

Polydactylism has occasionally been observed among other malformations as following Mendelian laws. Fotherby, Tubby, Lewis, and Embleton described such occurrences. In two cases that came under my observation I was able to trace the malformations through four and three generations respectively.

In the first case there are supernumerary fingers on both hands. The individual, a girl, aged fourteen years, was under my care for neurotic manifestations. A prolonged and careful inquiry of the parents and relatives revealed the presence of physical peculiarities with regard to fingers in many members of this family. I was able to obtain data on four generations.

First generation.

Great-grandparents—both normal.

Second generation.

Grandfather had six fingers on the right hand, but not on the left. Grandmother normal. One brother of the grandfather had six fingers on both hands. Two sisters were normal.

Third generation of eight children: Father had six fingers on both hands.

Four male children—normal.

Three female children—six fingers on both hands.

Mother normal.

Fourth generation—family of parents: Eleven children.

Five boys—normal.

Four girls—six fingers on both hands.

Two girls—six fingers on one hand, and in both cases on the right hand.

Of all the females my patient is the only one living. The other girls and three boys died at an early age from various acute infectious diseases.

The radiograph of the patient's hands shows a difference in

[1] Quart. Jour. Med., 1908, p. 331.

the origin of the supernumerary finger in either hand. On the right side the fifth and sixth metacarpal bones have one common base, the sixth is considerably shorter than the fifth. On the left hand the fifth and sixth metacarpal bones are equal in length. Besides, the first and second phalanges of the sixth finger are bent at a right angle and are ankylosed. It was impossible to determine with any degree of accuracy whether the last deformity as well as the mode of origin of the sixth finger existed in any other member of any of the fourth generations. The family came to this country from Austria. The grandfather was an Austrian, the grandmother French. With the exception of my patient, who was born in this country, all were born in Austria. No consanguinity could be traced in any of the marriages.

An analysis of the several generations from the standpoint of the abnormality shows the presence of a remarkable correspondence to Mendelian requirements. Beginning with the second generation there was one parent affected and the other unaffected. The polydactylism behaved as a dominant factor. The marriage of the person having this dominant with a normal resulted in children of about equal numbers, affected and unaffected.

In second generation we find:

Two males affected.

Two females unaffected.

In third generation:

Four males—normal.

One male affected.

Three females affected.

In fourth generation:

Five males—normal.

Six females—affected.

The fact that in the first generation both parents were normal does not disprove the fact that the abnormality did not exist. It evidently existed but in a potential form and segregation of the characteristics apparently commenced in the second generation. This phenomenon is identical to what we have seen in plants (see above).

It is also interesting to observe the phenomenon of sex-limitation in our case. Beginning with the third generation the females appear to present the largest number of individuals affected with the abnormality. The above-discussed role of sex in inheritance finds its support in the interesting manifestation of our case.

The second patient was an imbecile, fifteen years of age, who presented polydactylism in his feet. Each foot had six toes; the fifth, or last metatarsal bone of the right foot, is very thick and its large head is continued by two toes (fifth and sixth). On the left foot the fifth metatarsum is divided in its middle portion into two branches, which give off two toes (fifth and sixth). It took considerable time and labor to investigate the family tree of this patient. The result of the inquiry was very gratifying from the Mendelian standpoint. I was able to trace the deformity only in three generations, but not all the members presented it simultaneously in both feet.

First generation: Grandfather had six toes on the right foot and the toes were much longer than those of the left foot. His two brothers were normal.

He had no sisters.

Grandmother—normal.

Second generation:

Father—deformity in both feet.

Two brothers—deformity in both feet.

One sister—deformity in right foot.

Three sisters—normal.

Mother—normal.

Third generation:

Patient—affected (both feet).

Two brothers—affected on right foot.

Two brothers—affected on both feet.

Four sisters—normal.

These families were all Italians. The father emigrated to this country two years ago with his children, all born in Naples. The brothers died at an early age soon after they reached the United States. They were mentally somewhat below normal; two had

epilepsy. The mother had several miscarriages. A Wassermann test made on the patient's serum two years ago proved to be positive. The patient died from pneumonia six months ago. No consanguinity was present in the parents.

An analysis of the cases from the standpoint of Mendelian inheritance shows the polydactylism to behave as a dominant. I was unable to establish the presence or absence of the dominant factor beyond the first grandparents. In the latter the polydactylism is present in all intensity. In the second generation we find about the same number of affected and unaffected individuals (4 to 3). In the last generation the proportion is 5 to 4.

Besides polydactylism, other varieties of finger and hand malformation have been observed as playing the role of dominant and following Mendelain laws of inheritance. Brachydactyly, for example, was reported by Farabee[1] and Drinkwater.[2] The first observed through five generations shortening of fingers and toes which had only one phalangeal articulation. The second author traced the same peculiarity in seven generations.

Cases of "spalt-hand und spalt-fuss," traced through several generations were first described by W. Kümmel.[3] The deformity consists of the existence of a deep cleft in hand or foot, each of which contains two fingers or two toes, respectively, between which the cleft is situated. An excellent account of such deformities as well as of other defective conditions associated with this deformity, such as syndactyly or ectrodactyly is given by T. Lewis and L. Embleton.[4] They collected 180 individuals through five consecutive generations. More recently K. Schlatter[5] reported 19 cases of syndactyly in 33 members of one family in the course of four generations. The family transmission of the deformity seemed to conform to Mendel's law of inheritance.

More recent investigations show that certain diseases have been

[1] Peabody Museum of Amer. Arch. and Ethnol., Harvard Univ., 1905, iii, 3, p. 69.
[2] Proceed. Royal Soc. Edinburgh, 1908, xxviii, 35.
[3] Bibliotheca Medica, 1895, Abtheil. E., Hft. 3,
[4] Biometrica, March, 1908, v, vi, Part 1, p. 26.
[5] Correspondenz-Blatt f. Schweizer Aerzte, February 21, 1914.

traced in several generations of the same family and followed quite closely Mendelian's plan. Thomsen's disease, pseudo-hypertrophic muscular paralysis, retinitis pigmentosa, diabetes, hemophilia are the few affections which have been studied from this standpoint.

More elaborate studies have been made on transmission of morbid hereditary features in mental deficiency and psychoses. The most interesting account is presented in recent contributions by G. L. Cannon and A. J. Rosanoff,[1] and by A. J. Rosanoff and F. I. Orr.[2] They all examined a very large number of pedigrees of patients in Kings Park State Hospital with utmost care. Comparing their statistical data with the theoretical possibilities according to Mendelian laws one is struck with the remarkable correspondence between the two. Six different matings are considered by them and the conclusions to which this study leads are most significant. In view of their practical, viz., sociological interest, they deserve to be emphasized.

1. Both parents being normal and of pure normal ancestry, all children will be normal and not capable of transmitting the neuropathic make-up to the offspring.

2. When both parents are neuropathic all children will be neuropathic.

3. One parent being normal, but with a neuropathic taint from one parent, and the other parent being neuropathic, half the children will be neuropathic and half normal, although capable to transmit the neuropathic tendency to their offspring.

4. One parent being normal and of pure normal ancestry and the other parent being neuropathic, all children will be normal but capable of transmitting the abnormal tendency to offspring.

5. Both parents being normal but each with a neuropathic taint from one parent, one-fourth of the children will be normal and not capable of transmitting the neuropathic tendency to offspring, one-half will be normal but capable of transmitting the neuropathic make-up; the remaining one-fourth will be neuropathic.

[1] Journal of Nervous and Mental Disease, 1911, p. 272.
[2] Amer. Jour. of Insanity, lxviii, 221.

6. Both parents being normal, one of pure normal ancestry, the other with a neuropathic taint from one parent, all the children will be normal, half of them capable and the other half incapable of transmitting the neuropathic tendency to offspring.

An analysis of the results obtained from crossing plants or from mating animals possessing certain characteristic units, observations on transmission of bodily defects and malformations as polydactyly or brachydactyly, of certain diseases, of mental deficiencies and of neuropathic tendencies, such as described above, analysis of all these accumulated data points strongly to the existence in the original parent germ cells of a definite factor or determines which possess the power of transmitting certain characteristic units. What these factors actually are, in the light of our present knowledge, we are as yet unable to say, but we do know their potentiality. We know that they are capable to transmit certain color, certain shape, certain make-up of mind. The differences in individuals and species are unquestionably due to those same factors. Moreover, the facts related above demonstrate with evidence that hereditary transmission is accomplished according to strict laws and in a regular manner. No individual can transmit to the offspring a character-unit which he or she has not possessed.

This knowledge of inheritance tends to prove that the old conception concerning variation of individuals and species is not tenable. For the same reasons the Darwinian principle or natural selection as being the main cause of the variability of plants and animals does no more hold a solid ground. Neither the idea of survival of the fittest in the struggle for life can give the clue to the existence of the great variability of races and individuals.

Mendelian laws of heredity prove in my opinion beyond doubt that variation is the result of special crossings in which addition or loss of special characteristic units plays the most essential role. The importance of dominance and recessiveness cannot be overestimated. Once the special units of character exist, they are permanent and cannot be obliterated. Their segregation is only a distribution, but they invariably come out in subsequent

generations. Species and their variations depend exclusively on special crossings. Consequently variation of individuals and races is a definite occurrence based on definite combinations of segregated character-units. The conception of evolution therefore can no more admit a gradual transformation of individuals by gradual additions of imperceptible changes, but it must admit that these changes are controlled by physiological laws and that each new apparently additional character has in reality existed in the germ cell of the individual. These newer ideas of biological diversities which are founded on physiological observations and analytical breeding lead us directly to great possibilities in the domain of genetics and consequently to eugenics.

It is evident that the composition of members of society can be predicted and therefore controlled. Elimination of undesirable strains by forbidding marriage of individuals possessing them, encouragement of marriages of individuals with desirable elements, these are the two sociological problems that should appeal to an enlightened community. We know that consanguineous marriages tend to transmit to the offspring the same defective character-units which both parents possess in their germ plasm. Beginning with the second generation multiplicity of abnormal children may thus be created. As society has the right to protect itself, it certainly possesses all the prerogatives for forbidding marriages among relatives. Especially strong interference should take place in consanguineous marriages among feeble-minded, alcoholic and syphilitics. But if matrimony has not been prevented, the normal offspring should be directed to marry only normal individuals possessing a normal pedigree, but not to select their mates indiscriminately. If the abnormal offpsring cannot be prevented from marrying, they should be directed at least to marry normals possessing a normal pedigree. By these precautionary measures we mate two individuals one of whom is characterized by absence of the special determiner which is capable to produce a certain neuropathic or otherwise abnormal characteristic unit. Thus the pedigree in these cases will present a considerable sparseness as far as neuropathic elements are concerned. Castration in both

sexes and vasectomy are other measures which enable us to prevent the production of generations of abnormal types. Much has been said in certain quarters against them but the voices raised come from individuals who were either prompted by sentimental motives or else are not familiar with the laws of heredity as described above, with the power of transmission of character-units once they originate in the germ cells, with the constancy and regularity of this transmission. Segregation of persons with a marked neuropathic inheritance during the reproductive period of life is still another prophylactic measure in our endeavors for disappearance of abnormal character-units in successive generations and therefore for improvement of our race.

The foregoing analysis of our knowledge of laws of heredity directs us physiologically, so to speak, to the proper understanding of breeding or crossing. Herein lies the fundamental principles of formation of certain characteristic features of individuals and races and of the manner with which varieties and species arise. The entire phenomenon of heredity is merely a phenomenon of individuals and controlled by precise and specific physiological laws. A profound knowledge of the principle of inheritance enables one to grasp the fact that the character of the component elements of human society can be greatly controlled. Consequently the proper conception of eugenics is the direct outcome of this fundamental knowledge.

A STUDY OF THE COMPARATIVE TOXICITY OF THE VARIOUS PREPARATIONS OF MERCURY[1]

WITH A HISTOLOGICAL STUDY OF EXPERIMENTAL MERCURIAL NEPHRITIS

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For more than four centuries mercury has been employed in the treatment of syphilis. It has had, perhaps more than any other medicament, varying vicissitudes of fortune, being highly lauded as a soverign remedy in one period and condemned as a vicious poison in the next. At times the toxic effects of the drug and the malign effects of the disease against which it was used were sadly confused in the medical as well as in the lay mind. It fell from time to time into disrepute and desuetude, only later to be reinstated as a valuable medicament. During the greater part of the nineteenth century the main reliance in the treatment of syphilis was placed in mercury. When Ehrlich announced the elaboration of salvarsan as a superior remedy for spirochetic infections it appeared for a while as if mercury in this disease would finally be consigned to the oblivion of obsolete drugs. Arsenobenzol is a remarkable chemical combination. The clinical results that have been achieved by its use are well known to all; those, however, who have employed it in laboratory

[1] Read February 3, 1915. Presented in part before the Annual Meeting of the American Dermatological Association, May, 1915.

animals against trypanosome and spirochetic infections are forced to marvel at the results obtained when compared with other known remedies. Its high affinity for these parasites and its low affinity for the body cells make it therapeutically efficacious and at the same time of relatively low toxicity.

Syphilographers generally are of the opinion, however, that the best results in the treatment of this disease are to be accomplished by the use of both salvarsan and mercury. While it is presumed that mercury, like salvarsan, acts as a spirocheticide, yet we have no direct evidence of such action in experimental animals. The parasiticide effect of salvarsan on trypanosomes and spirochetes in the blood can be readily demonstrated; on the other hand, the destructive influence upon these organisms in the test-tube is much feebler than that of mercury. Mercury is the best germicide known in the test-tube, but when injected into the blood of experimental animals infected with trypanosomiasis or with the spirochete of relapsing fever it has no demonstrable effect upon the parasite and does not materially delay death from these diseases. We know definitely, however, that mercury has a curative influence upon the lesions of syphilis, just as has iodin which possesses no spirocheticide effect. The manner of action of salvarsan and mercury, therefore, may be somewhat different, and the latter is still to be regarded as an approved remedy in the treatment of syphilis.

Mercury may be introduced into the system by a variety of routes, by alimentary administration, by inhalation of mercury vapor, by inunction through the skin, and by injection beneath the skin, into the muscles or directly into the blood stream. Prof. Welander, of Stockholm, claims that a considerable part of the effect presumed to result from inunctions is due to volatilization of the mercury on the skin and absorption through the lungs. He therefore devised certain mercury bags to be worn about the neck. Mercury is eliminated chiefly through the intestines and the kidneys, the greater part being excreted through the former. The most efficacious results from the use of mercury in syphilis are obtained from the employment of massive doses,

as would naturally be expected, such doses are likewise the most dangerous for the individual by reason of damage to the excretory organs, particularly the kidneys. Within recent years syphilographers have more particularly relied upon inunctions and injections of mercury as the best methods of administering the drugs. The special mercurial preparations employed by injection have been selected largely on the basis of convenience and relative freedom from pain produced, rather than because of any known superiority of one salt over another.

The most frequently employed soluble mercurial salts are the bichloride, benzoate, succinimide, oxycyanate, cyanide, sozoiodolate, and cacodylate. The chief insoluble mercurial preparations in use are the salicylate, calomel, and gray oil.

We have devoted much time to the elaboration of new organic mercurial compounds and the testing out of the same on animals for their toxic and therapeutic effects. In the determination of the toxicity of the various new compounds prepared by us, it was found desirable to compare it with that of the mercurial salts in use. This led to the inquiry which is detailed in this communication.

Immediate Lethal Dose. A rapid method of testing the toxicity of the various salts is the determination of the immediate lethal dose. For this purpose intravenous injections of a solution of the drug were given to rabbits, repeated injections being administered at intervals of one or two minutes until death ensued. In all cases death resulted within ten minutes. Below is appended a table giving the amount of the mercurial salt per kilo of body weight, the percentage of mercury in each salt, and the actual amount of pure mercury per kilo administered.

DOSIS LETHALIS: TOXICITY OF MERCURIAL SALTS

	Immediate lethal dose, gm.	Contained mercury, per cent.	Amount of pure mercury, gm.
1. Hg. salicylate	.027	58	.0155
2. Hg. sozoiodolate	.024	32	.0077
3. Hg. cacodylate	.37	20	.0075
4. Hg. benzoate	.015	45	.0067
5. Hg. bichloride	.007	74	.0052
6. Hg. oxycyanide	.0055	83	.0045
7. Hg. succinimide	.007	50	.0035

The Dosis Tolerata. In order to determine for practical use the comparative toxicity of the various soluble preparations of mercury administered intravenously, we endeavored to ascertain the dosis tolerata of the different salts. In these experiments groups of eight to ten white rats were injected with graded doses of each salt varying, as a rule, from $\frac{1}{4}$ mg. to 8 mgs. per kilo of body weight. The dose was dissolved in 1 c.c. of water and the injections were given into the exposed jugular vein. The animals were numbered and tagged and each group set aside in special cages to determine the maximum dose that could be given without inducing a fatal result; this dose is the dosis tolerata.

Great difficulties were encountered in arriving at the tolerated dose of the different salts owing to inconsistencies in the results. It not infrequently occurred that a rat receiving .0004 gm. of the drug would survive while those receiving .0002 and .0003 gm. would succumb. Every effort was made to render the technic of the experiments as perfect as possible. The drugs were carefully weighed on delicate balances in the chemical laboratory and were dissolved in such quantity of water as would make for the greatest accuracy of dosage. The intravenous injections were given after the jugular vein had been exposed; in this manner the dose to the fraction of a drop was introduced into the circulation.

In order to reduce the chances of error to a minimum, each experiment was repeated several times. For instance, each mercurial salt in graded doses was tested out intravenously on a series of rats on three different occasions. During our studies on the toxicity of the mercurials we employed 259 rats and 20 rabbits. Despite the precautions taken, and the repetition of the experiments, inexplicable variations in the findings occurred. We have become convinced that biological experiments of this character cannot be carried out with the expectation of mathematically precise results.

The only reason that we can assign for the variant results is that inherent differences exist in the resistance of the individual rats to poisonous drugs.

DOSIS TOLERATA: INTRAVENOUS INJECTIONS

	Hg. bichloride. Hg. = 74 per cent.			Hg. benzoate. Hg. = 45 per cent.				Hg. succinimide. Hg. = 51 per cent.			
Rat No.	Weight.	Dose. §	Death after days.	Rat No.	Weight.	Dose. §	Death after days.	Rat No.	Weight.	Dose. §	Death after days.
1	126	.0008	1	1	90	.0008	3	1	65	.0008	3
2	88	.0007	5 min.	2	107	.0007	4	2	98	.0007	4
3	117	.0006	30	3	68	.0006	5	3	70	.0006	5
4	77	.0005	5	4	99	.0005	14	4	81	.0005	0
1 a	61	.0005	2	5 a	85	.0005	4	9 a	87	.0005	14
5	134	.0004	34	5	116	.0004	5	5	103	.0004	5
2 a	74	.0004	3	6 a	82	.0004	4	10 a	59	.0004	4
6	68	.0003	6	6	61	.0003	0	6	070	.0003	14
3 a	76	.0003	0	7 a	79	.0003	5	11 a	59	.0003	0
7	87	.0002	0	7	89	.0002	0	7	108	.0002	13
4 a	97	.0002	0	8 a	63	.0002	0	12 a	58	.0002	0
8	87	.0001	0	8	92	.0001	0	8	78	.0001	14
9	93	.00005	0	9	110	.00005	0	9	115	.00005	4
10	71	.000025	31	10	97	.000025	0	10	77	.000025	27

a Second experiment.
§ Dose per 100 gms. body weight.
0 Animals thus designated did not die during the period of observation of about two months.

	Hg. cacodylate. Hg. = 20 per cent.			Hg. Hg. = 32 per cent.				Hg. salicylate. Hg. = 45 per cent.*			
at No.	Weight.	Dose. §	Death after days.	Rat No.	Weight.	Dose. §	Death after days.	Rat No.	Weight.	Dose. §	Death after days.
1	57	.0008	8	1	58	.0008	5	1	56	.0008	3
7	105	.0007	3	2	82	.0007	3	2	60	.0007	2
13	85	.0006	30	3	65	.0006	27	3	94	.0006	2
1 a	70	.0006	19	24	81	.0005	0	4	57	.0005	3
14	87	.0005	0	6 a	138	.0005	19	13 a	..	.0005	3
2 a	72	.0005	0	5	60	.0004	2	5	76	.0004	3
15	95	.0004	27	7 a	124	.0004	16	14 a	..	.0004	0
3 a	104	.0004	22	6	115	.0003	4	6	69	.0003	4
15	88	.0003	0	8 a	84	.0003	31	15 a	..	.0003	0
4 a	96	.0003	0	27	119	.0002	0	17	67	.0002	0
7	75	.0002	0	9 a	111	.0002	23	16 a	..	.0002	0
5 a	128	.0002	12	8	98	.0001	0	18	55	.0001	0
8	102	.0001	19	66	94	.0005	7				
9	59	.00008	11	76	86	.0004	0				
1 c	69	.0006	7	86	66	.0003	23				
2 c	87	.0005	0	96	92	.0002	16				
3 c	105	.0004	20								
4 c	71	.0003	14								
5 c	71	.0002	0								

§ Dose per 100 gms. body weight.
a Second experiment.
c Third experiment.
* In the first experiment Hg. salicylate was dissolved in piperazin water; in the second the same drug was dissolved in weak alkali.
0 Animals thus designated did not die during the period of observation, which lasted about two months.

DOSIS TOLERATA: INTRAVENOUS INJECTIONS

Hg. oxycyanide. Hg. = 83 per cent.				Hg. oxycyanate. Hg. = 45 per cent.			
Rat No.	Weight.	Dose. §	Death after days.	Rat No.	Weight.	Dose. §	Death after days.
1	57	.0008	2	1	82	.0008	At once.
2	59	.0007	13	2	54	.0007	At once.
3	50	.0006	At once.	3	84	.0006	Few minutes.
4	72	.0005	At once.	4	90	.0005	Few minutes.
5	67	.0004	0	5	70	.0004	Few minutes.
10 a	62	.0004	1	6	57	.0003	1
6	65	.0003	3	7	75	.0002	1
11 a	64	.0003	5	8	79	.0001	0
7	104	.0002	5	9	81	.00005	0
12 a	67	.0002	1				
8	89	.0001	0				
13 a	62	.0001	0				
9	71	.00005	0				
10	79	.000025	0				

a Second experiment.
§ Dose per 100 gms. of body weight.
0 Animals thus designated did not die during the period of observation of about two months.

DOSIS TOLERATA: INTRAMUSCULAR INJECTIONS. SOLUBLE COMPOUNDS

Hg. bichloride. Hg. = 74 per cent.				Hg. benzoate. Hg. = 45 per cent.				Hg. succinimide. Hg. = 51 per cent.				Hg. salicylate. Hg. = 45 per cent.*			
Rat No.	Weight.	Dose.	Death after days.	Rat No.	Weight.	Dose.	Death after days.	Rat No.	Weight.	Dose.	Death after days.	Rat No.	Weight.	Dose.	Death after days.
1	86	.0012	4	6	92	.0012	4	11	71	.0012	35	16	85	.0011	3
2	101	.001	4	7	81	.001	21	12	70	.001	36	17	82	.001	4
3	83	.0008	0	8	102	.0008	49	13	81	.0008	0	18	108	.0008	24
4	65	.0006	34	9	71	.0006	34	14	84	.0006	0	19	81	.0006	4
5	66	.0004	34	10	70	.0004	30	15	73	.0004	19	20	72	.0004	0
								11a	183	.0012	0				
								12a	150	.001	0				
								13a	135	.0008	0				
								14a	99	.0006	0				
								15a	190	.0004	0				

* Dissolved in weak alkali.
a Second experiment.
0 Animals designated thus did not die during the period of observation of about two months.

The deaths of animals occurring between the third and fourth week cannot be properly ascribed to the injection of the drug, as control rats not infrequently die after such a period without discoverable cause.

In expressing the dosis tolerata of the various salts administered intravenously, we have taken the average tolerated dose of three series of experiments. In the subjoined table is given the amount of the salt per kilo of body weight and the amount in terms of pure mercury per kilo, that could be borne without fatal result.

DOSIS TOLERATA: INTRAVENOUS INJECTIONS

	Amount of drug per kilo, mgs.	Pure Hg. per kilo, mgs.
Hg. salicylate	3.0	1.7
Hg. bichloride	2.0	1.5
Hg. benzoate	2.4	1.1
Hg. succinimide	1.8	.9
Hg. cacodylate	4.5	.9
Hg. oxycyanide	1.0	.83
Hg. sozoiodolate	2.2	.75

In this series of experiments the salicylate of mercury dissolved in weak alkali, and the bichloride could be given in somewhat higher dosage (in terms of pure mercury) than the other salts, although the differences were not very striking.

Two and a half milligrams of bichloride per kilo of body weight is the highest dose that can be given intravenously without causing death. This would be equivalent to $2\frac{1}{2}$ grains for a person weighing 120 pounds.

Dosis Tolerata by Intramuscular Injection. The soluble salts of mercury being given chiefly by intramuscular injection, an effort was made to determine the dosis tolerata by this mode of administration. The figures given in the following table represent the average of three series of experiments:

	Amount of drug per kilo.	Pure Hg. per kilo.
Hg. succinimide	14.0	6.0
Hg. bichloride	6.5	4.8
Hg. sozoiodolate	12.0	4.0
Hg. benzoate	8.5	3.8
Hg. cacodylate	18.0	3.6
Hg. salicylate	4.0	2.5

The succinimide was best borne in this series of intramuscular injections, the bichloride of mercury coming next.

The Relation of the Intramuscular to the Intravenous Dose. It is interesting to note the amount of mercurials tolerated by intramuscular administration as compared with direct injection into the blood stream. This is best established by determining the ratio of each salt and then averaging these to determine the difference in the amount of mercury tolerated by these two routes. Computation discloses the fact that about *four times more mercury can be borne by intramuscular administration than by intravenous infusion.*

DOSIS TOLERATA: INTRAMUSCULAR INJECTIONS. INSOLUBLE COMPOUNDS

Calomel. Hg. = 85 per cent.				Gray oil. Hg. = 100 per cent.				Hg. salicylate. Hg. = 45 per cent.			
Rat No.	Weight.	Dose.	Death after days.	Rat No.	Weight.	Dose.	Death after days.	Rat No.	Weight.	Dose.	Death after days.
1	56	.016	14	10	75	.01	14	1	72	.014	5
9	74	.016	18								
2	81	.01	20	17	90	.01	17	2	73	.011	5
3	101	.008	17	11	77	.008	18	3	63	.0095	4
4	56	.006	21	15	70	.008	0	4	78	.005	0
10 a	60	.006	6	12	65	.006	20	5	97	.002	0
5	101	.004	22	16 a	66	.006	0	6	97	.001	0
11 a	69	.004	0	13	99	.004	30	7	73	.001	0
6	93	.002	21	17 a	70	.004	23	8	110	.0005	13
12 a	68	.002	0	24	90	.002	0	9	166	.0002	0
7	65	.001	21	18 a	69	.002	0	10	68	.0003	0
13 a	61	.001	0	15	38	.001	0				
8	104	.0005	10	19 a	69	.001	30				
24 a	61	.0005	30	16	79	.0005	22				
				20 a	60	.0005	0				

a Second experiment.
0 Animals thus designated did not die during the period of observation of about two months.

Repeated Intramuscular Injections. When soluble preparations of mercury are administered for their therapeutic effect to human subjects they are given as a rule intramuscularly either daily or triweekly. In order to reproduce the conditions of a human experiment, ten rabbits were placed under daily intramuscular injections. Five of the most commonly employed mercurial salts were selected—the bichloride, benzoate, salicylate, succinimide and cacodylate. Each drug was used upon two rabbits. The purpose of this experiment was to determine the comparative

toxicity of these salts by observing the effect on the kidneys and by noting the duration of life of the rabbits. The rabbits were catheterized on alternate days and the urine carefully examined for albumin. The daily dose at first employed was about 0.001 mg., but was subsequently increased to 2 and again to 4 mgs.

DAILY INTRAMUSCULAR INJECTION OF MERCURIAL SALTS

Rabbit number.	Name of the chemical.	Total amount received per kilo in gms.	Total amount in terms of Hg. per kilo in gms.	Duration of life. Days.
6.	Mercuric bichloride	.071	.052	45
7.	Bichloride	.028	.021	31
8.	Hg. succinimide	.033	.017	33
9.	Hg. succinimide	.071	.035	45
10.	Hg. benzoate	.042	.018	34
11.	Hg. benzoate	.014	.006	14
12.	Hg. salicylate	.015	.008	17
13.	Hg. salicylate	.071	.041	44
14.	Hg. cacodylate	.118	.023	44
				Alive after two months
15.	Hg. cacodylate	.091	.018	48

In this experiment, which extended over a period of more than forty-eight days, the individual variation in the experimental animals is again evident: one bichloride rabbit, for instance, was able to stand daily injections totalling 71 mgs. before succumbing, whereas its mate died after receiving 28 mgs. In view of this variability of resistance we would hesitate to draw positive conclusions as to the relative toxicity of the different mercurial salts employed. However, the experiment is not without value, for certain deductions may be drawn therefrom. It is perfectly evident that the bichloride of mercury was no more toxic than the other salts in use; indeed, in terms of pure mercury contained this drug was in this experiment borne better than any of the other preparations.

Recent investigators have maintained that inorganic mercurial salts, in which mercury exists as an ion, are organotropic and therefore more highly toxic. The explanation is that in inorganic mercury salts, the mercury ion being free, combines with the proteins of the body. The other salts employed in this experiment, the succinimide, benzoate, salicylate and cacodylate, are

what is known as half-complex organic compounds, in which the element mercury is no longer free as an ion, but is in combination with organic substances. Such mercury compounds do not attack proteins as vigorously and therefore are regarded as less toxic.

The results of the experiment under discussion do not bear out the views just referred to. This may be due to the fact that in the half-complex salts employed the mercury was combined in such loose form that it was readily split off in the body and combined with cellular proteins. It is interesting, too, to observe the maximum amount of bichloride of mercury that could be tolerated in fractional doses over a long period of time. Rabbit 6 received 70 mg. of mercury per kilo in forty-five days; this would be equivalent to 70 grains for a person weighing 120 pounds. The amount given was to be sure toxic and caused progressive loss of weight. At the onset the rabbit weighed 1934 grams, whereas at the time of its death, forty-four days later, it weighed about 1228 grams. Albumin was present in the urine from time to time, but only in traces and during most of the period the urine was free of albumin.

Rabbit No.	Urinary findings. Day upon which albuminuria was first observed.	Day of death.	Histological changes in kidneys.
6.	Sixth day	45	Slight tubular nephritis; no calcareous deposits.
7.	Eleventh day	31	Slight exudative glomerulonephritis with proliferative changes; slight tubular nephritis. No calcareous deposits.
8.	Ninth day	33	Acute intertubular and glomerular condition with slight tubular nephritis; no calcareous deposits.
9.	Thirty-second day	45	Slight tubular nephritis; no calcareous deposits.
10.	Sixth day	34	Slight tubular nephritis; no calcareous deposits.
11.	Sixth day	14	Acute intertubular and glomerular congestion with glomerular exudate and early proliferate changes; slight tubular nephritis; no calcareous deposits.
12.	Eighth day	17	Slight tubular and glomerular (exudative) nephritis; no calcareous deposits.
13.	Sixteenth day	44	Slight tubular nephritis; early intracapillary glomerulonephritis; no calcareous deposits.
14.	Thirty-second day	Alive after two months.	
15.	Tenth day	48	Slight tubular and glomerular (exudative) nephritis; no calcareous deposits.

Insoluble Mercurial Preparations. The insoluble preparations of mercury are at the present time employed to a greater extent than the soluble.

We endeavored to institute a comparison of the toxicity and rapidity of absorption of calomel, gray oil, and the salicylate of mercury. Five white rats received respectively 6, 4, 2, 1.5 mgs. of *calomel* into the gluteal muscles. The animal receiving 6 mgs. (the equivalent of 60 grains for a person weighing 120 pounds) died on the sixth day. The animal receiving 0.5 mg. died on the thirtieth day. The other rats survived. Six rats received respectively 8, 6, 4, 2, 1.5 mgs. of *gray oil.* The animal receiving 4 mgs. (the equivalent of 40 grains for a person weighing 120 pounds) died on the twenty-third day. The other rats survived. In a second experiment nine rats received doses varying from 16 mgs. to 0.5 mg. of *calomel.* All the animals succumbed between the fourteenth and twenty-second days. Eight rats received doses varying from 10 mgs. to 0.5 mg. of *gray oil.* All of the animals succumbed between the fourteenth and thirtieth days except two that received 2 and 1 mg. respectively. Ten rats received respectively 14, 11, 9, 5, 2, 1, 0.5, 0.25 mgs. of *salicylate of mercury* in oil suspension. Those receiving the three highest doses died within one hundred and twenty hours, the other rats survived. Five milligrams (the equivalent of 50 grains for a person weighing 120 pounds) was therefore the tolerated dose.

Three rabbits of approximately the same weight were, on October 20, given intramuscularly, respectively 16 mgs. of calomel, 16 mgs. of gray oil, and 10 mgs. of salicylate of mercury. The first two doses are the equivalent of about 8 grains of the drug for a person weighing 120 pounds. The urine was frequently examined for albumin; none was present at the end of sixteen days; a second dose of 8 mgs. of each of these drugs was given on November 2. The day following, albumin and casts appeared in the urine of each rabbit, but subsequently disappeared.

On November 19 the calomel and gray oil rabbits received a third injection of 16 mgs. and the salicylate rabbit 10 mgs. On December 1 a fourth injection of 180 mgs., an enormous dose,

was given to each rabbit. The calomel rabbit died on December 2, having lived forty-four days. The salicylate rabbit died on December 7, having lived forty-eight days, and the gray oil rabbit died on December 17, having lived fifty-six days. The calomel and salicylate rabbits died after a severe diarrhea. The gray oil rabbit had no diarrhea but albumin was present in the urine for a number of days before death. The salicylate rabbit lost most in weight, the calomel rabbit moderately; the gray oil rabbit gained in weight.

Experiment on the Comparative Rapidity of Absorption of Gray Oil, Calomel, and Salicylate of Mercury. Three rabbits were injected respectively with a single dose of 180 mgs. of mercury in the form of gray oil, 180 mgs. of calomel, and 180 mgs. of salicylate of mercury.

These preparations were carefully incorporated in creamy suspensions, 1 c.c. of which was injected into the muscles of the thigh. This dose is the equivalent of about 90 grains of the drug for a person weighing 120 pounds. The *gray oil rabbit* died at the end of forty-nine days. The muscle into which the injection was made was excised and analyzed for the amount of unabsorbed mercury; 86 mgs. were recovered, representing 48 per cent. of the amount injected. The *salicylate rabbit* died at the end of forty-five days. Forty-eight milligrams of mercury were recovered from the muscle. Inasmuch as mercury salicylate contains but 58 per cent. of mercury, the amount of pure mercury injected was 104 mgs.; *the quantity remaining as unabsorbed therefore was 46 per cent. of the amount of mercury injected.*

The *calomel* rabbit died at the end of twenty-one days. Calomel contains 85 per cent. of mercury; therefore 180 mgs. would represent 153 mgs. of the pure metal. Of this amount, 108 mgs. were recovered. *Therefore 71 per cent. of mercury was unabsorbed at the end of twenty-one days.* The rate of absorption of gray oil was 1.05 per cent. per day; the rate of absorption of salicylate of mercury was 1.2 per cent. per day. The rate of absorption of calomel was 1.4 per cent. per day. These figures indicate a remarkable uniformity in the rapidity of absorption of these

preparations. The slightly higher figure for calomel may possibly be explained by the shorter life of the rabbit, for one would naturally expect a relatively greater absorption during the early days of the experiment as this experiment very clearly demonstrates a direct relationship between the amount of mercury absorbed, the amount of mercury injected, and the number of days it has lain in the tissues. It also indicates that metallic mercury incorporated in gray oil is absorbed as readily as calomel or the salicylate of mercury. This is surprising inasmuch as calomel and salicylate of mercury represent combinations in which mercury has already undergone oxidation, whereas gray oil contains the unoxidized metal.

In a second experiment, two rabbits were injected with 180 and 153 mgs. of calomel respectively, and the third with 180 mgs. of gray oil. These animals were killed at the end of twenty-one days and the mercury unabsorbed in the muscles recovered and the amount determined. The results were much the same as in the first experiment, three-quarters of the mercury being found still present in the muscular tissue. The figures are set forth in the following table:

SINGLE INTRAMUSCULAR INJECTION IN RABBITS

Drug.	Amount of drug injected in terms of mercury, mg.	Day of death, days.	Per cent. of Hg. not absorbed.	Rate of absorption per day, mg.
Calomel	180	21 (died)	90.0	.90
Calomel	180	21 (killed)	78.4	1.85
Calomel	153	21 (killed)	71.0	1.40
Gray oil	180	21 (killed)	75.0	2.14
Gray oil	180	49 (died)	48.0	1.06
Hg. salicylate	104	45 (died)	46.0	1.20

General Discussion of Results. While we have indicated in various tables our findings concerning the relative toxicity of the soluble mercurial salts we hesitate to draw therefrom any too definite conclusions. As has been stated, rats exhibit considerable variations in their resisting power to mercurial intoxication. We have endeavored to limit the experimental error as much as possible by using a large number of animals and averaging the results. One of the most important findings of our experiments

is that the *toxicity of* the various mercurial salts is, in a general way, proportionate to the amount of pure mercury contained in the salt. In order to be sure of the amount of mercury in the salts used in our experiments, special analyses of each salt were made by us. The mercurial preparations vary greatly as to their mercurial content. The bichloride, for instance, contains 74 per cent., whereas the sozoiodolate contains but 32 per cent. The cacodylate of mercury could be given in the largest quantity and at first sight appeared to be the least toxic. We have heard that certain clinicians are able to administer this drug in larger dosage than other mercurial salts. According to its theoretical formula the cacodylate should contain 42 per cent. of mercury. Repeated analyses made by us of Merck's product show, however, that it contained but 20 per cent. In terms of pure mercury, therefore, its toxicity does not differ materially from that of other mercurial salts.

Our experiments demonstrate that the organic mercurial compounds are not perceptibly less toxic than inorganic salts. This is doubtless due to the fact that the organic compounds in use are in very weak combination. This indeed can be shown by the facility with which their mercury is split off from the organic rest by ammonium sulphide. In order to produce less toxic mercurial compounds it is necessary that the mercury be attached to two carbons C – Hg. – C, so that the element is fixed and no longer able to enter into combination with the proteins of the body. None of the half-complex organic compounds investigated by us appear to be materially superior to the bichloride of mercury. By intravenous injection the tolerated dose of this salt is 2 mgs. per kilo of body weight, the equivalent of 2 grains for a person weighing 120 pounds. By intramuscular administration the tolerated dose was in the neighborhood of 6 mgs. per kilo, the equivalent of 6 grains for a person weighing 120 pounds. This figure which represents an enormous dose must not be accepted as an amount that could be safely injected, for some rats succumbed to this dose. Larger doses were, however, at times tolerated and 6 mgs. per kilo was borne by most of the animals.

In administering the insoluble mercurial compounds animals must be kept under observation for very long periods of time to judge of the effect of the drug given. We have injected into rats 4 to 6 mgs. of calomel or gray oil (the equivalent of 40 to 60 grains for a person weighing 120 pounds) and the rats have been well at the end of a month; but ultimately they die of the effects of the injection.

One hundred and eighty milligrams of mercury in the form of gray oil, and 180 mgs. each of calomel and the salicylate of mercury (the equivalent of 90 grains for a 120-pound person) were injected into three rabbits; the latter survived as long as seven weeks. The daily rate of absorption we have calculated to be between 1 and 1.5 per cent. This slow absorption explains why the insoluble mercurials may be given in relatively large doses. The *mercury contained in them is just as poisonous as in the soluble salts, but it is yielded up to the circulating fluid at a very slow rate.* A word of caution must here be sounded for the insoluble mercurials; administered as they usually are, once a week, they are sure to accumulate in the body. We have shown that about 50 per cent. of the mercury remains unabsorbed in the body, even as late as six or seven weeks after injection. The effect of weekly injections therefore is progressively cumulative. Mercury is powerfully renotropic and the kidney is the first organ to show damage from the toxic effects of the drug. We have often seen albuminuria and casts develop in patients receiving insoluble injections at weekly intervals. There are on record in the literature a large number of deaths from the use of insoluble mercurials. These preparations have certain advantages over the soluble salts but are far more dangerous and should be reserved for use by the experienced and careful clinician.

Mercury Nephritis. *A Histological Study.* A large proportion of the experimental animals succumbing to mercurial intoxication were autopsied and histological examinations made of the various organs, particularly the kidneys. In this manner we were able to study the changes produced in the kidneys after the administration of various salts by intravenous and intra-

muscular injections and at intervals varying from twenty-four hours to as long as six weeks after injections.

The nephritis produced by mercury is primarily a tubular form of nephritis. In mild intoxications the histological changes may be confined almost entirely to the convoluted tubules. In practically all but these mild intoxications, however, some changes are to be found in the glomerules characterized mainly by a serous or hemorrhagic exudate into the capsular spaces. Only exceptionally were examples of true intracapillary glomerulonephritis encountered and well-marked capsular changes were found only occasionally and in the subacute and chronic intoxications. The vascular changes were never extreme and usually consisted in congestion of the veins in the midzonal and cortical portions. In general, therefore, it may be stated that in mild degrees of mercurial poisoning the resulting nephritis is essentially a tubular nephritis; in all severer intoxications (and these include all that are fatal within a week or ten days after administration of the salt) the nephritis is a combination of severe tubular and hemorrhagic glomerular nephritis.

These histological changes may now be described briefly but in more detail.

The Tubular Lesions. As already stated, these are usually in evidence in sections of kidneys from all rats and rabbits succumbing to mercurial intoxication after a longer or shorter interval. *Even in those animals receiving small and non-fatal doses of mercury but autopsied after an interval of six or seven weeks, well-defined changes were apparent in the tubules.*

These changes in the tubular epithelium are to be attributed to a direct toxic degeneration of the cells by mercury rather than an inflammatory process resulting from elimination of a toxic substance. For this reason there are usually slight or no evidence of leukocytic infiltration in or about damaged tubules; we have, however, in three animals found the reverse condition, namely, a well-marked infiltration of the peritubular tissues and intratubular collections of leukocytes mainly of the mononuclear variety, plasma cells and a few esinophilic cells. This condition

has been called acute interstitial non-suppurative nephritis and is ascribed by Mallory to the diffusion of mercury in the intertubular tissues with absorption along the lymphatics.

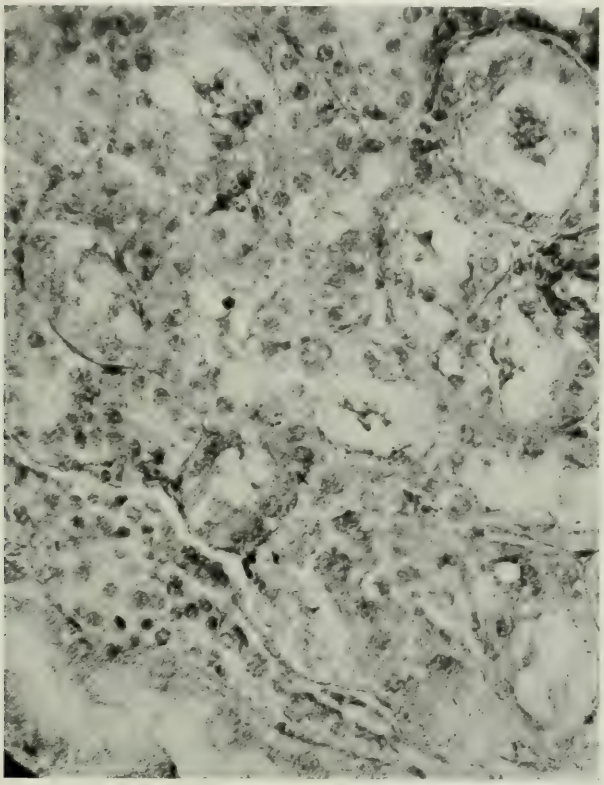


FIG. 1.—Mercury nephritis. Early tubular changes. Kidney of a rat removed twenty-four hours after the intravenous administration of 0.006 gram per kilo of body weight of bichloride of mercury.

Tubular changes may be apparent within twelve to twenty-four hours after the administration of a fatal dose of a soluble salt. The early changes were found to consist of swelling and fragmentation of the lining cells of the tubules; the nuclei are clouded and show varying degrees of degenerative changes and the lumina

of the tubules are filled with necrotic desquamated cells or casts of serum and networks of fibrin (Fig. 1).

Frequently, and especially in intoxications that are fatal within a few days, well-marked edema of the tubules in the cortical portions are apparent; in these instances the tubules are found widely distended with fluid and the lining cells flattened (Fig. 2).

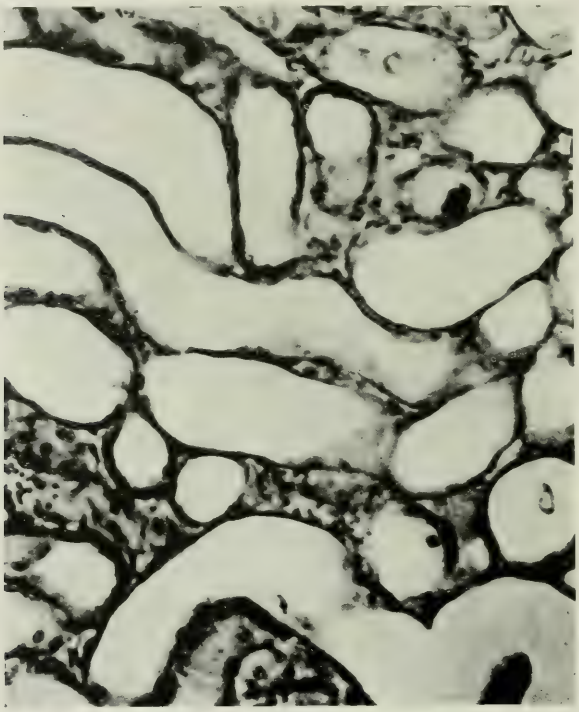


FIG. 2.—Mercury nephritis. Extreme edema of tubules in the cortex of the kidney of a rat removed twenty-four hours after the intravenous injection of 0.003 gram per kilo of body weight of oxycyanide of mercury.

The convoluted tubules are mostly involved. The midzonal portions of the kidney or that portion just on or about the midline between the cortical and medullary sections of the kidney, show the best-marked and severer lesions. It is apparent, therefore, that mercury is chiefly eliminated by both the proximal

and distal portions of the convoluted tubules, the loops of Henle and straight collecting tubules not being selectively engaged and usually escaping injury. This is particularly apparent in the straight collecting tubules. Occasionally certain tubules seem

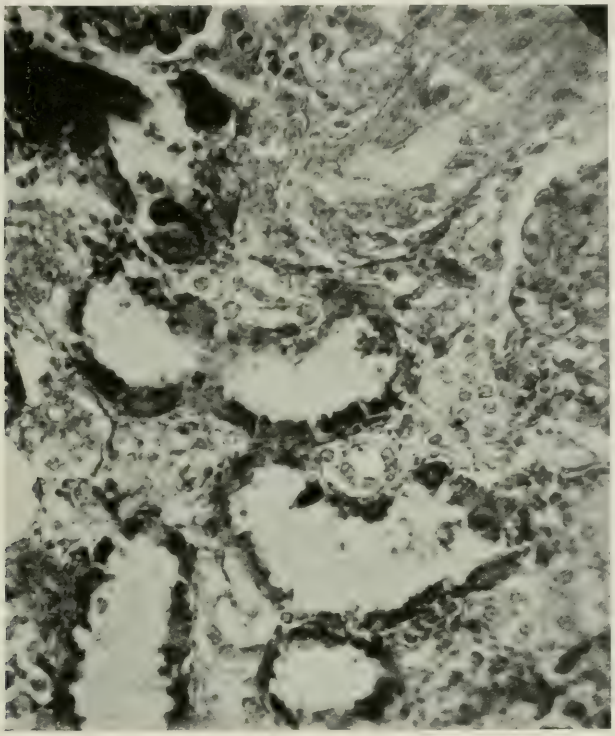


FIG. 3.—Mercury nephritis. Severe tubular nephritis with calcification. Kidney of a rat five days after the intravenous injection of 0.003 gram per kilo of body weight of salicylate of mercury in piperazin water.

to be selected and are the sites of extensive involvement while neighboring tubules are relatively intact.

Casts are usually present. In early lesions these are serous or composed of networks of fibrin. Desquamated epithelial cells are frequently found collected in masses in the lumina of tubules. Not infrequently the tubules are filled with blood.

Casts may be present in any portion of a tubule, but are especially in evidence in the convoluted and straight collecting portions.

Calcification has been found as early as forty-eight hours after the intravenous injection of a soluble salt. This infiltration is first apparent in those tubules involved and begins in the basement membrane of the tubules. Soon the attached cells become

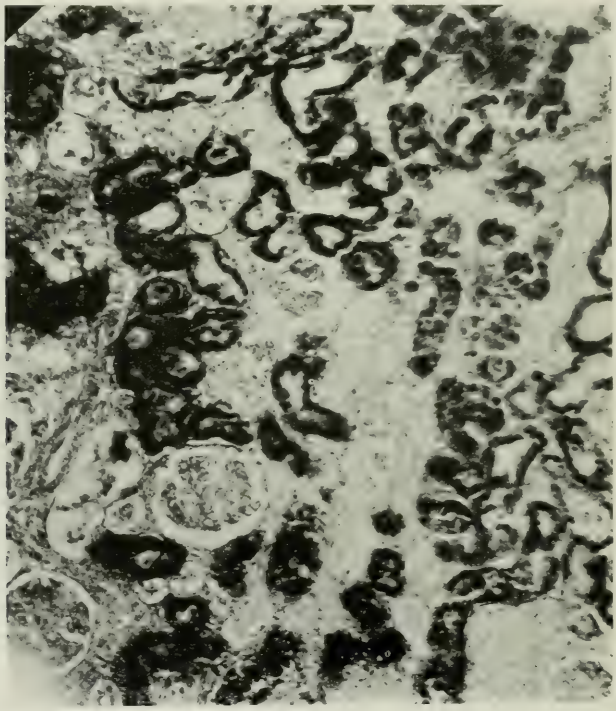


FIG. 4.—Mercury nephritis. Kidney of rat removed seventy-two hours after the intravenous injection of 0.003 gram per kilo of body weight of succinimide of mercury.

infiltrated and when desquamated, casts of cells infiltrated with the calcium salts are found in the tubules.

Calcification is most apparent in the midzonal region and first appears in this area; later and in severer intoxications all the tubules in the cortical and midzonal regions are involved with characteristic and extensive damage to the tubules (Figs. 3 and 4).

Ordinarily the glomerules escape this process of infiltration with calcium salts; in these experimental lesions, however, we have found three kidneys showing deposits of small amounts of calcium in the glomerules.

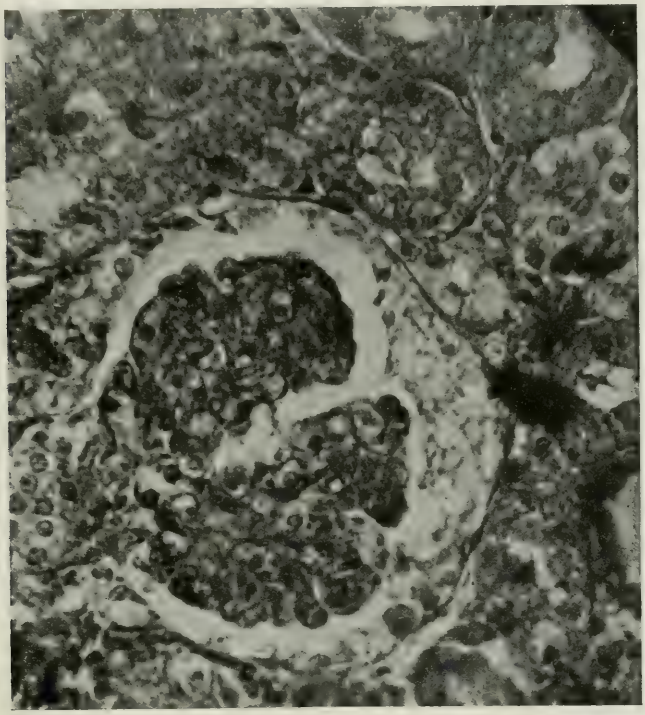


FIG. 5.—Mercury nephritis. Exudative (hemorrhagic) capsular glomerulonephritis. Kidney of a rat removed forty-eight hours after the intravenous injection of 0.003 gram per kilo of body weight of succinimide of mercury. Note tubular nephritis with early calcification.

Glomerular Lesions. As previously stated, animals receiving small and non-fatal doses of mercury may show no appreciable gomerular lesions. As will be pointed out later, however, the great majority of our animals succumbing to mercurial intoxication showed some glomerular involvement along with the tubular changes.

The common glomerular lesion is an acute capsular glomerulonephritis of the exudative type. The exudate is usually hemorrhagic and the nephritis therefore may be called an acute hemorrhagic glomerulonephritis.

The capsular spaces are usually widely dilated and frequently appear empty, the serous exudate having drained away. Occasionally, however, a network of fibrin enmeshing desquamated lining cells and a few leukocytes is to be found in the capsular space.

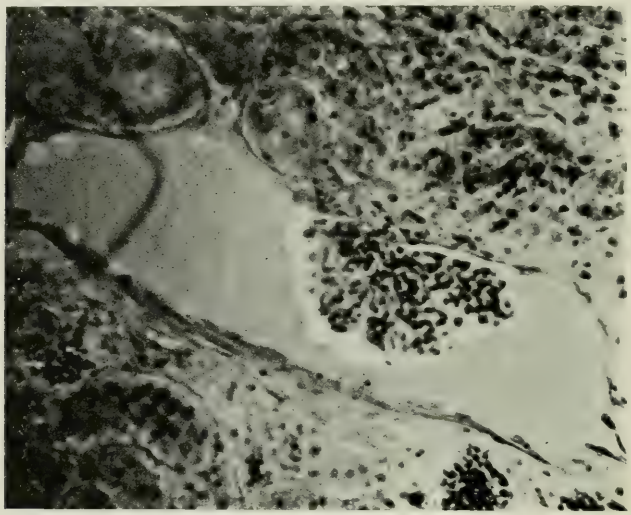


FIG. 6.—Mercury nephritis. Exudative (serous) glomerulonephritis. Kidney of a rat removed twenty-four hours after the intravenous injection of 0.002 gram per kilo of body weight of oxycyanide of mercury.

The usual and more typical finding, however, is a collection of blood in the capsular space (Figs. 5 and 6). The number of leukocytes present is always small except in these occasional instances of acute interstitial non-suppurative nephritis when general leukocytic infiltration is a marked feature.

Proliferative changes were occasionally encountered. In these instances there was found well-marked desquamation of the lining epithelial cells of the capsular space with evidences of

epithelial regeneration and a distinct thickening of the capsule with connective tissue. These lesions were found among the subacute and chronic intoxications and were exceptional rather than frequent.

Likewise well-marked examples of intracapillary glomerulonephritis were uncommon in our series. As already stated, the usual glomerular lesion was characterized by marked edematous distention with a hemorrhagic exudate. In severe intoxications, however, necrosis of the cells of the tuft was evident and also an enlargement of the glomerulus with an increased number of nuclei due to leukocytic infiltration. The normal lobulation of the tuft was somewhat obscured, due to congestion of the capillaries.

As already stated we have occasionally found early calcification of the tuft but in no instance was this process well marked.

Relative Frequency of these Lesions. The lesions found in the kidneys of one hundred animals succumbing to mercurial intoxications are summarized as follows:

A. Of 68 animals receiving a single intravenous injection of a *soluble salt* of *mercury* in dose varying from 0.001 to 0.008 gm. per kilogram of body weight and succumbing in from one day to six weeks the following lesions were found:

1. Tubular nephritis in all (100 per cent.).
   Mild in 14, or 20 per cent.
   Severe in 54, or 80 per cent.
   Calcification in 36, or 52 per cent.
2. Exudative glomerulonephritis in 57, or 68 per cent.; calcification of the glomeruli was noted in 3 of these.

B. Of 32 animals receiving single or multiple doses of insoluble salts of mercury in amounts totalling from 0.01 to 0.18 gm. per kilogram of body weight and succumbing in from five days to seven weeks the following lesions were found:

1. Tubular nephritis in all (100 per cent.).
   Mild in 14, or 44 per cent.
   Severe in 18, or 56 per cent.
   Calcification in 9, or 30 per cent.

2. Exudative glomerulonephritis in 18, or 56 per cent.

3. Proliferative glomerulonephritis in 3, or about 10 per cent.

It is apparent that with the slower absorption of insoluble salts of mercury from the muscle the tubular lesions are less severe, calcification is less in evidence and a tendency to chronic or proliferative changes more in evidence.

Relative Toxicity of the Salts of Mercury According to Kidney Changes. Accepting severe tubular nephritis with calcification as a criterion for judging the relative renotoxicity of the various salts of mercury the following summary may be made:

A. Soluble salts administered intravenously in dose varying from 0.001 to 0.008 gm. per kilogram of body weight.

Salicylate of mercury (in piperazin water)	100	per cent.	severe	tubular	nephritis.
Succinimide of mercury	71	"	"	"	"
Benzoate of mercury	33	"	"	"	"
Bichloride of mercury	25	"	"	"	"
Cacodylate of mercury	25	"	"	"	"
Sozoiodolate of mercury	25	"	"	"	"

The oxycyanide and oxycyanate of mercury are not included, as these salts killed our animals within twenty-four hours; while well-marked diffuse nephritis was produced, calcification was not in evidence.

B. Soluble salts of mercury administered intramuscularly in dose varying from 0.005 to 0.02 gm. per kilogram of body weight:

Salicylate of mercury (in piperazin water)	100	per cent.	severe	nephritis.
Succinimide of mercury	83	"	"	"
Bichloride of mercury	30	"	"	"
Benzoate of mercury	30	"	"	"
Sozoiodolate of mercury	0	"	"	"
Cacodylate of mercury	0	"	"	"

Judging, therefore, purely on the basis of the severity of the kidney lesions by histological examination, the salicylate of mercury proved most toxic for the kidney epithelium, succinimide of mercury coming second.

C. Insoluble salts of mercury administered intramuscularly in single dose varying from 0.01 to 0.18 gm. per kilogram of body weight:

Salicylate of mercury	. . . . .	60 per cent.	severe	nephritis.
Gray oil	. . . . .	50 "	"	"
Calomel	. . . . .	31 "	"	"

Conclusions. 1. Rats exhibit such variation in their resisting power to mercurial salts that too much weight should not be attached to minor difference in toxicity in the experimental findings.

2. While the maximum tolerated dose of the various salts may be widely divergent, when the doses are calculated in the terms of pure mercury, they fall within relatively narrow limits.

3. In general terms, it may be stated that the toxicity of the various mercurial salts is directly proportionate to the amount of pure mercury contained.

4. The inorganic salts, as represented by the bichloride of mercury, are no more toxic than the numerous organic combinations that are commonly employed.

5. The differences in the molecular structure of the mercury compounds tested by us were found to be of relatively little importance as affecting their toxicity.

6. The bichloride of mercury was on the average fatal in intravenous doses above 2 mgs. per kilo of body weight; administered intramuscularly, it was fatal on the average above 6 mgs. per kilo of body weight.

7. The average relationship as to the toxicity between the intravenous and intramuscular administration of mercury, in general, was about 4 to 1.

8. The insoluble preparations such as gray oil, calomel and the salicylate of mercury are absorbed at the rate of a little over 1 per cent. of the injected amount per day.

9. Even at the end of six or seven weeks, almost 50 per cent. of the mercury of insoluble preparations may be unabsorbed at the site of the injection.

10. The injection of the usual doses of insoluble mercurial compounds at weekly intervals must invariably lead to accumulation of the drug in the tissues.

11. Insoluble mercurial injections should be given only by the skilled physician after careful consideration of the dose and of the intervals of administration.

12. Mercury has a great affinity for the cells of the kidney, and this organ is one of the earliest involved in mercurial intoxication. Hence during the intensive treatment with mercury the necessity of careful examination of the urine from time to time should be emphasized.

13. The nephritis produced by mercury is primarily tubular in variety; capsular glomerulonephritis of the exudative (hemorrhagic) variety is frequent and practically always accompanies severe tubular nephritis. Calcification of the degenerated tubular cells has been found within forty-eight hours after the administration of mercury and always occurs in severe mercury nephritis irrespective of the salt administered or the route of injection.

DISCUSSION

Dr. H. A. Hare: I think the gentlemen presenting this subject have rendered a distinct service, not only by this contribution of original work, but in calling attention to a fact which those of us who have had our attention centred upon this matter have long recognized and which has not been generally recognized by medical men, namely, that the mercurials are dangerous in the acute and subacute types of nephritis to such an extent that for a goodly number of years I have always before administering mercurials, except possibly small doses of calomel, followed the dosage by salines, sweeping them out. I have always seen to it that the urine was examined microscopically, and if red blood cells were present or there was the slightest evidence of acute lesions in any part of the kidney, I put mercury aside with even greater rigor than I would put arsenic aside if some such combination of drugs had been suggested for the case. I think this is a point to which very few physicians pay much attention. It was impressed upon my mind particularly by a case

of syphilitic nephritis, due to virulent syphilitic infection, in which the patient suffered from hematuria and in which the history was that on three occasions when given mercurial injections the hematuria greatly increased and the man suffered great pain over the kidneys. It was just about the time of the introduction of salvarsan. Salvarsan was not considered in the case, and I remember that the physician in charge argued that the condition of the kidney prevented the elimination of the mercury, saying very truly that nothing could save the man's life, and he did die.

The so-called cumulative effect of mercury, I think, also does not receive the attention it should. Most of us in our student days were taught to push the mercury until the gums became touched, and then the dose was cut down to one-half, the so-called tonic dose, and continued at that dose, unless the evidence of syphilis became more virulent, in which case the dose was run up a second time. This was in recognition of the so-called accumulation of mercury in the body. Those familiar with the literature concerning the process which mercury undergoes in the body, however, recognize that the progress of its elimination is exceedingly slow, and, therefore, we should be all the more cautious in its employment. I think Dr. Schamberg touched upon one point in this matter which is of great importance in regard to a good many of the drugs. It affects the employment of the cacodylates in syphilis in which almost no arsenic is set free. If it be true that when the insoluble mercurials are given hypodermically they remain undissolved and unelim-inated, it is also true that they cannot exercise the powerful antisyphilitic influence that many persons now give them credit for.

In regard to the slides shown by Dr. Kolmer, and solely for information, and not because I have any idea of error in his technic, I would like to ask whether he has made sections of kidneys in other animals than rats and rabbits, and whether in such other animals, and perhaps in human kidneys, this deposition of calcium salts occurs everywhere? I remember that Dr. Welch, of Johns Hopkins University, found that when certain poisons were administered to some cats careful examination of the kidneys revealed wide-spread fatty deposits around all the secreting portions of the kidney. This was considered to be due to fatty degeneration induced by the drug, whereas, every cat has a zone of fat around its Malpighian tufts. I should like to know whether the condition is peculiar to those animals, or whether it is practically universal.

The general recognition on the part of the profession, subsequent to the publication of this article, that mercury is by no means an innocuous drug; that mercury has a selective renal affinity, as Dr. Schamberg has so well said, and that the insoluble preparations considered so innocuous

and safe, are not innocuous on the one hand, and not particularly safe on the other, adds very materially to its importance.

Dr. Robert N. Willson: Touching upon the point mentioned by Dr. Hare, it occurs to me that it may be of interest to report to the College two cases of uremia occurring on the wards of the Philadelphia General Hospital, both of chronic interstitial nephritis, and both resulting from the administration of about two grains of calomel. One died in uremia. The other recovered from a fully developed state of uremia. I have also studied with interest a third case, one of pericarditis in a young colored boy who received by error 64 grains of calomel within three days. That boy also died, and microscopic sections from his kidneys showed the typical verscalete niene of the Germans, very much the same condition as that seen in the kidneys of the rats shown by Dr. Kolmer. I have a large number of specimens made in Vienna from the kidneys of patients treated in the luetic wards with mercury, all of which show the same type of kidney. During the last two or three weeks I had the privilege of seeing with Dr. Jump, a young woman who presented a curious combination of cardiac and neurasthenic symptoms, but whose apparently normal kidneys functionated perfectly so far as we could determine. Shortly after the administration of a small dose of calomel she vomited, the urinary flow ceased, she went into uremia, and died. This is the fourth case which I have personally studied inside of a brief period, poisoned by small doses of calomel. These occurrences have an especial interest in the light of a statement made to me recently by an old lady who grew up in the South, to the effect that in her younger days she was frequently given a teaspoonful of calomel at a dose; and that it was not an infrequent thing for the physicians to prescribe even larger doses of the drug.

Dr. David Riesman: I should like to ask Dr. Schamberg whether a soluble preparation of mercury when injected into the tissues does not become an insoluble preparation by being transformed into an albuminate. I should also like to ask whether he has considered inunctions both as regards their therapeutic efficacy and as regards the amount of mercury actually absorbed, and whether there is any local storing up of mercury in the tissues. It seems to me that when it is well rubbed in it disappears. Are inunctions not a better way of introducing the mercury than injecting a soluble or insoluble preparation? I am glad Dr. Schamberg has called attention to the harmfulness of the overuse of mercury in nephritic cases. I do not think that a small blue pill does any harm, but repeated doses of mercury have a bad effect. Many physicians in Philadelphia are fond of prescribing in heart disease the Niemeyer pill, which contains a grain of calomel. Given in cases of cardiac dropsy without coincident Bright's disease, very good results are obtained; but when given in dropsy

of nephritic origin, the Niemeyer pill does harm. Personally, I do not use it when the albuminuria is nephritic and not merely due to passive congestion of the kidneys. As this particular point is, however, not always easily determined, a certain amount of caution must be observed.

Dr. James M. Anders: I think the paper of the essayists is a particularly instructive one, and one calculated to make us more cautious in the hypodermic use of preparations of mercury. I should like to ask Dr. Schamberg whether, as a result of his observations on the lower animals or on patients, he can recommend any special preparation of mercury for hypodermic use. I understood him to say that the salicylate belonged to the insoluble group of mercurial salts. This is the preparation that I have been in the habit of employing hypodermically with, as I have had reason to believe, excellent results, although in some cases, at least, inunctions gave even better results. I would also ask him what would be the proper interval between the injections in view of the cumulative effects of the drug.

Dr. Kolmer (closing): Dr. Hare's question, I think, is answered very well by the remarks of Dr. Willson. It is true that the changes shown in the kidneys of the rabbit and rat from fatal mercury intoxication occur also in the human kidney. Owing to lack of time, I omitted to throw on the screen a photomicrograph of such a fatal case showing similar changes in the human kidney after death caused by mercury.

Dr. Schamberg (closing): The injection of a soluble salt of mercury into the tissues would, as Dr. Riesman suggests, doubtless lead to the formation of an insoluble compound; but this must be more or less rapidly reconverted into a soluble combination, else it could not be carried through the blood stream, influence the tissues therapeutically, and be eliminated through the kidneys. It must in the end become soluble no matter what the primary local change is. I believe that inunctions constitute the safest method of employing mercury in massive doses. Prof. Welander, of Stockholm, claims that much of the effect of mercurial inunctions is due to absorption of the mercury by the lungs that there is a volatilization from the skin, with inspiration through the respiratory tract. It has been shown that patients placed in the same room with those anointed with mercury likewise absorb the drug. Concerning Dr. Anders's inquiry of the best preparation of mercury to be employed for injection, I may say that the conclusions which we have given do not necessarily apply to the human subject.

I think insoluble mercury compounds ought never be injected oftener than once a week. If the dose is large, not oftener than every two weeks. One grain of salicylate of mercury per week would not damage the kidneys. Careful examination of the urine should be made from time to time in

patients who are receiving mercury. Curiously in rabbits that received daily intramuscular injections of mercury over a period of forty-eight day, the kidneys showed microscopic pathological changes after autopsy, although during life albumin was only irregularly present in the urine. I think that the medical profession is not sufficiently awake to the fact that mercury is a powerful kidney irritant.

The great storehouse of mercury is the liver, just as the liver stores up salvarsan and other drugs. The two organs for which mercury has the greatest selective affinity are the liver and the kidneys. This is not necessarily because it is eliminated through these organs, for there are other drugs so eliminated, but because mercury is powerfully renotrophic. I recall a patient whom I saw with Dr. John W. Swan some years ago, who received at the hands of another physician mercury by inunction, by injection, and by mouth, at the same time for a supposedly luetic eruption. She developed a severe nephritis with anasarca, and Dr. Swan, who analyzed her urine daily, found that she continued to eliminate the drug for 127 days after the last dose of mercury had been ingested.

THE THYMUS AND PITUITARY IN DEMENTIA PRECOX AS PHYSIOLOGICAL CHARACTERISTICS IN INSANITY[1]

By S. D. W. LUDLUM, M.D.

In the cases of dementia precox, Abderhalden reactions were obtained in some instances to testicle and pancreas, and in others to testicle and thyroid, while in still others no reaction whatever could be obtained. In the group of individuals that gave the reaction to testicle and pancreas certain physiological characteristics were observed. The physical symptoms present were leukopenia, increased blood-pressure, a feeble and rapid pulse, a temperature 2° above normal, exaggerated deep reflexes, diminished cutaneous reflexes, increased electrical reaction of muscles, tremor of tongue and extremities, an apparently good state of nutrition, the Westphalz-Pilcz pupillary sign, increased mechanical irritability of the muscles, and dermatographia. The symptoms noted in this group are only a few compared with the total number of symptoms described in the symptom-complex of dementia precox, but they seem to form a group of patients differing in their physiological characteristics from the others classified as dementia precox.

X-ray examination of the bones in this group of patients showed an apparent loss of calcium, certainly less than is found in the usual run of patients.

In looking over the various books of internal secretion we found that the symptoms described as resulting in animals after

[1] Read February 3, 1915, (by invitation).

the extirpation of the thymus were almost identical with those occurring in the patients that gave the Abderhalden reaction to testicle and pancreas.

At the Johns Hopkins Hospital, through the kindness of Dr. McClure, it was possible for us to secure blood at different times, from two thymectomized animals, with controls. The dog whose thymus had been out a year gave a positive reaction to testicle and pancreas. The other dog whose thymus had been out eighteen months gave a positive to testicle and a doubtful reaction to pancreas and spleen. None of our patients have ever given any reaction to spleen. At any rate, both the dogs and the group of six patients gave the same Abderhalden reactions, and exhibited the same physiological symptoms.

Pathologically, Parhon and Zugravu, in the *Archive de Neurolgie*, November, 1913, note in dementia precox hypertrophy of the suprarenals. Dercum and Allis[1] observe, also a considerable increase in the size of the suprarenals in some cases of dementia precox. Studying the reported inter-relationships in the literature we wish to draw attention to the fact that the inter-relationship as shown by Paton's diagram is an excellent working basis for this sort of study. For instance, if we remove the thymus, inhibition is removed from the spleen and pancreas, as well as testicles; and that the Abderhaldens in the patients reacted to testicle and pancreas, and in Simon's cases done at the Sheppard and Enoch Pratt Hospitals 95 per cent. at least reacted to testes. It would appear that we are beginning to arrive at a ground from which we can approach the study of these patients from a more satisfactory viewpoint than the psychological one.

Waldeyer, in 1890, insisted that thymus parenchymatous tissue remains until old age. This has been confirmed by Hamar and Lerch.[2] It is quite settled there is a close relationship between the thymus and thyroid and the sex organs. Castration causes hypertrophy, while great sexual activity hastens the involution of the thymus, as in young animals, which leads naturally to the

[1] Journal of Nervous and Mental Disease, February, 1913.
[2] Medical Record, April 27, 1914.

inquiry as to the effect of masturbation in producing dementia precox. Involution of the thymus has an exhilarating effect on sex glands. We find enlarged thymus in status thymolymphaticus, Grave's disease, and Addison's disease. Halstead points out in his latest article on exophthalmic goitre that there is an increase in the relative lymphocyte count when the thymus is enlarged.

We found in our precox cases from this thymus group that there was a relative decrease, as well as absolute decrease, in the number of lymphocytes. All these cases showed a leukopenia. When we treated them with Lundvall's prescription of sodium nucleinate and arsenious acid injected under the skin, we found that we could make a leukocytosis and a relative lymphocytosis. This treatment, in our hands, did no especial good; although the theory of it may be quite correct; for Dr. Walter Jones in his last work "Nucleic Acids: Their Chemical Properties and Physiological Conduct," states that the only nucleic acids that we know anything about are the thymus nucleic acid and the yeast nucleic acid.

We treated several of our patients with thymus-gland extract, and out of 6 cases, 3 gave excellent results and are presumably well at the present time. The other cases were old and much demented, so that one could hardly expect the treatment to have very good results; but we believe that if a patient with the physiological symptoms mentioned above, and with a characteristic blood-pressure record, is treated early a very definite result can be obtained.

In going over the cases that gave no Abderhalden reaction, we found that there was another group. They had a very low blood-pressure (sometimes as low as 90). The pressure on having the patient stand, went below the figure named when they were lying down, instead of rising eight to ten points, as it should have done, when they stood up. Their deep reflexes were diminished and sometimes absent. Their temperature was subnormal, often by two degrees. There was lessened activity in electrical reaction. Pigmentation of the skin was noted. The testicles were small and atrophied; the genital hair scanty. The pulse was slow, the

bowels markedly constipated. There was a history of repeated attack of grippe or rhinorrhea. A general muscular and mental asthenia was noted, the patient acting like a case of precox without the emotional outburst. He was dull, more or less stupid and apathetic; orientated and with but slight delusion.

Such a case is hard to differentiate from a case of dementia precox; but it has the physiological characteristics of the cases described as dyspituitarism.

In addition to these forms, there is a hyperpituitary mental condition that has its prototype in a mentally retarded girl of five years, who has the stature of eight years. Her serum reacts only to the pituitary gland, and she represents the beginning of gigantism. This prototype is followed by cases in adults who exhibit unusually large skeletal growth, and sometimes reversal of sex development, with the mental symptoms of hypomania. The blood-pressure is usually very high.

Working on the assumption that this is hyperpituitary, and studying Paton's chart, we found that extract of testicle would inhibit pituitary activity. This we administered in 4 cases of this type; and the mental symptoms subsided after each injection, within twenty-four hours. They rose again; but repeated injections of Brown-Séquard fluid was followed by recovery in a short time. This does not mean that all cases of mania will recover under treatment of Brown-Séquard fluid, but only those of the type of hyperpituitarism.

A summary resumé of this paper would be that:

1. In a group of cases of dementia precox, Abderhalden reactions were obtained in some instances to testicle and pancreas; and in others, to testicle and thyroid; while in still others no reaction could be secured.

2. In the individuals that gave the reactions to testicle and pancreas, there were observed physiological symptoms of the same type as those found in animals from which the thymus had been removed.

3. In examining the blood of animals whose thymus had been removed, the same reactions obtained as in cases of a certain

group of patients, indicated that in this group there exists a disease entity.

4. With regard to the pituitary, there were a considerable number of cases with the symptoms of dispituitarism that improved with pituitary extract. There were also groups of cases of hyperpituitarism that improved with the opposite organic extract, which is the Brown-Séquard fluid.

DISCUSSION

Dr. John A. Kolmer: I think the work of Tampé and his co-workers showed that in exophthalmic goitre a more constant and intense reaction is obtained with exophthalmic goitre tissue than with normal thyroid, a conclusion that in this disease would point to perverted function of the gland rather than to a hyperfunction alone. I should like to know whether Dr. Ludlum has used precox tissues as substrata in any of his work as having a bearing upon this subject. I am also impressed with Dr. Ludlum's report regarding the benefits observed following the administration of various tissue extracts to precox patients. One important question raised by Fauser's original work in this subject referred to gland therapy, for if antisex gland ferments do occur in the circulation in dementia precox it may be assumed that digestion of these cells or cell products will take place *in vivo* and that a state of chronic protein intoxication may easily follow. If this were true then it would appear that the administration of extracts of these glands would aggravate the condition instead of impairing it, as reported this evening, unless we assumed that the so-called ferments are not capable of digesting normal gland tissue as that of a lower animal. At least the results reported this evening tend to show that organotherapy does not aggravate the condition and work of this character will probably yield more exact information in this particular field of therapy.

Dr. Ludlum (closing): I cannot speak definitely of the material used in our experiments because most of the laboratory work was done by Dr. Corson White. I would say, however, that there has been a great deal of criticism of the Abderhalden reaction as being not specific, and that some have reported positive results in males and negative in females in using the test for the diagnosis of pregnancy. The experiments made by Dr. White have been in every way trustworthy, and I feel that when the work is properly done it will be found that the results can be relied upon.

A REMARKABLE CASE OF HOUR-GLASS STOMACH, WITH PERFORATION OF AN ULCER[1]

By HOBART AMORY HARE, M.D.
AND
J. CHALMERS DaCOSTA, M.D.

The operation upon the patient was as follows: Incision over the left rectus. The abdomen was examined. Gall-bladder was small, shrunken, and free from adhesions. The stomach was found to have a constriction across it extending from the lesser to the greater curvatures. It divided the stomach into two sacs joined by an opening about large enough to admit the tip of the index-finger. The right sac was much the larger of the two and was greatly prolapsed. The pylorus appeared to be normal. The right sac was drawn over and anastomosed to the left sac, a large opening being made. Clamps were used during the application of the first row of sutures, but after the completion of this suture line the clamps had to be removed because of tension, which made it impossible to insert and tie the stitches. Had the left sac been a little smaller and a little higher up it would have been necessary to perform rib resection in order to have permitted the performance of the operation.

Two days after the operation the patient developed pneumonia. The following day the right lung was solidified and the patient became stuporous and died November 29.

DISCUSSION

Dr. H. A. Hare: Dr. DaCosta expected to be here, and give the operative details in connection with this case, but he is unable to be present. My name is connected with the case largely out of courtesy because the

[1] Read February 3, 1915.

patient was under my care. The patient was a man, aged about forty-eight or fifty, who suffered from severe pain in the upper zone of the abdomen. The diagnosis was obscure as to whether the condition was a malignant growth or ulcer. The *x*-ray photograph produced this very extraordinary manifestation of hour-glass stomach. It is difficult to conceive of a deformity greater than this which could be produced by disease. When I saw the *x*-ray plate I doubted the accuracy of Dr. Manges's diagnosis; everything seemed to me to be wrong about it. When the patient came to operation, however, and the tissues were laid bare the accuracy of the *x*-ray plate was proved. The stomach was seen with the eye actually in the body as represented by this photograph. The points which Dr. DaCosta expected to discuss were those of the proper surgical procedure in a case of this kind. As a matter of fact, he ignored the extravasation, except to close the perforation. He ignored the fibrous band which represented the annular constriction. He bridged the space between the upper and lower parts of the stomach by anastomosis. The man died three or four days following operation from pneumonia at the base of the lung on the side of operation. The *x*-ray picture is such an unusual one of hour-glass stomach that we thought the case worthy of presentation to the College. I regret that Dr. DaCosta is not here to discuss the problems in surgery which he wished to bring before the Fellows of the College.

RECENT PROGRESS IN THE PHYSIOLOGY OF THE PITUITARY BODY[1]

By ALFRED REGINALD ALLEN, M.D.

Although it is scarcely the province of this paper to deal with the anatomy, embryology and histology of the pituitary body, yet it were well to make a few statements covering some of the main points which later in our discussion will assume importance.

In human embryos of 3.2 mm., or about the end of the third week of embryonic life, the oral plate, separating the foregut from the stomodeum ruptures, but antedating this there has already appeared an invagination of the buccal ectoderm directly in front of the oral plate pointing upward toward the ventral cephalic fold. This pocket of ectoderm, known as Rathke's pouch, will come in contact with an evagination in the floor of the diencephalon at about the fifth week, and in this manner is formed the pituitary body, the pars anterior from Rathke's pouch, the pars posterior from the diencephalic pouch. The hollow stalk from the stomodeum to Rathke's pouch is soon obliterated, only a slight condensation of cells marking its position. The later formation of the sphenoid bone completes the obliteration. Persistence of the cells of this stalk in continuity from the pharynx to the sella is a great rarity. But remains of either end of the stalk have been frequently found. Erdheim called attention first to the persisting cells at the pharyngeal end and named it the *Rachendachhypophyse*. Arai, Dandy and Goetsch described the para-

[1] Read March 3, 1915.

hypophysis, which is most likely the remnant of the pituitary end of the stalk. Although the possibility of hyperplasia and tumor formation in these vestigeal sites must be recognized, yet the likelihood of their playing a physiological role is remote.

The further development of Rathke's pouch is evidenced in a great proliferation of the cells forming the anterior aspect of the vesicle. This soon causes a crescentic extension of the pouch posteriorly, which encircles more or less completely,

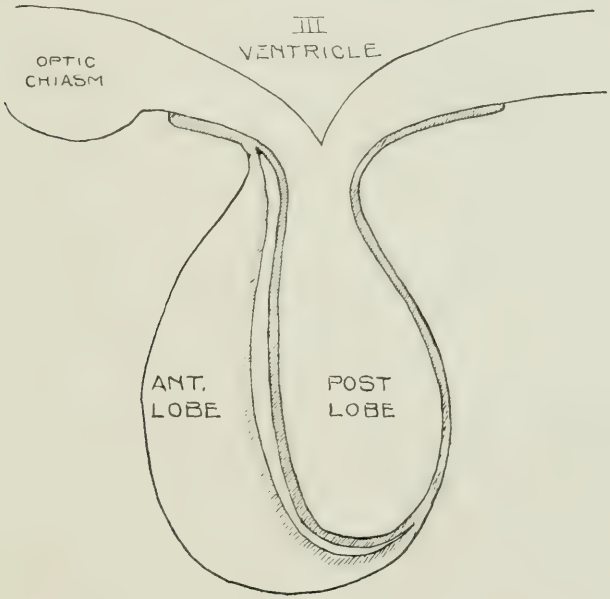


Fig. 1

according to the animal, the infundibular lobe. In the dog the pars posterior is often completely encircled not only in the region of the neck of the pars posterior but also about the posterior lobe itself.

Where the posterior wall of Rathke's pouch comes in contact with the pars posterior, the junction is morphologically so complete that we have fallen into the error of considering this posterior wall part of the pars posterior. Because of its appearance in

sagittal sections it is known as the pars intermedia (Fig. 1). Genetically the pars intermedia is part of the pars anterior and in no way a part of the pars posterior.

The original cavity of Rathke's pouch persists through life in man as well as in the dog and many other animals. In the child this cavity or the pituitary cleft, as it is called, is quite large and on postmortem examination is often found distended by a clear, colorless, jelly-like material which usually stains faintly basically, This material is found in the embryo as early as three and a half months. In the adult the cleft is not so pronounced.

Histologically the cells of the pars anterior may be divided into two groups: the chromophile cells and the chromophobe cells. The chromophile cells are either acidophilous in their staining when they are called eosinophiles or they are basophilous when they are called basophiles. The chromophobe cells, the *Hauptzellen*, show very slight, poorly staining cytoplasm, the outline of which is hard to determine. The nucleus of the chromophobe cell is large and contains a goodly amount of well-staining chromatin. In the male and virgin animal this often appears as a nucleus surrounded by indistinct granular matter. According to most histologists the arrangement of the cells in the pars anterior is definite and as follows: The polyhedral or round cells form cellular plugs between which pass the blood sinuses. Next to the blood sinus is found the chromophile cells. In the interior of the cellular plug are found the Hauptzellen. In the central part of the pars anterior the eosinophiles predominate, giving to the section stained by eosin-alkaline methylene blue a central red area. In the periphery of the pars anterior the basophiles are in excess, giving a blue coloration in the same specimen. Now, I have frequently found this condition but just as frequently have I found a total lack of any arrangement in pituitaries which were supposedly normal.

Whether the staining and morphological differences in these three types of cells indicate simply different stages of activity of the same kind of cell, as is held by Benda, cannot now be positively stated.

The pars posterior, outside of its bloodvessels and the surrounding moiety from the pars anterior and intermedia, is made up chiefly of neuroglia fibers and a few neuroglia nuclei. A few nerve fibers have been described by certain observers but are inconstant and doubtful findings.

Passing from the pars intermedia into the substance of the pars posterior are seen globules of secretion. These are at times free in the substance of the pars posterior and at times partly or

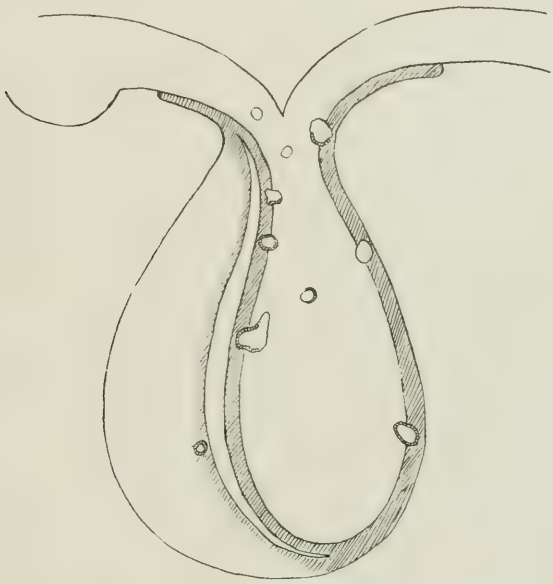


Fig. 2

completely surrounded by cuboidal cells. The ultimate destination of these globules is the infundibulum from which they are discharged into the ventricle cavity (Fig. 2). The nature of this secretion has not been determined. It is not colloid, in the sense of the thyroid secretion minus iodine. The thyroid colloid remains homogeneous after treatment with acetic acid while the pituitary globules swell and dissolve. This also differentiates the pituitary globule from mucin. I have found the secretion usually faintly

basic but occasionally acid, and in a number of human pituitaries both acid and basic particles in the same globule (Fig. 3).

It is the general opinion that this secretion comes from the pars intermedia, the posterior wall of the pituitary cleft. I would say that I have found these globules in the posterior part of the pars anterior and also in the extreme anterior part of the pars anterior (Fig. 4). The cuboidal cells surrounding the globule are often

Fig. 3.—Acid granules in field of basic secretion. (Mallory's aniline blue stain.)

ciliated, as can be seen in my preparations. This fact is not mentioned by most of the histologists. Ziegler refers to the ciliated lining of cavities in the posterior lobe.

I have also found ciliated epithelium lining the pituitary cleft. This fact of the cells of the pars anterior and intermedia having cilia is particularly interesting when we remember that at the time of the formation of Rathke's pouch the cells of the primitive

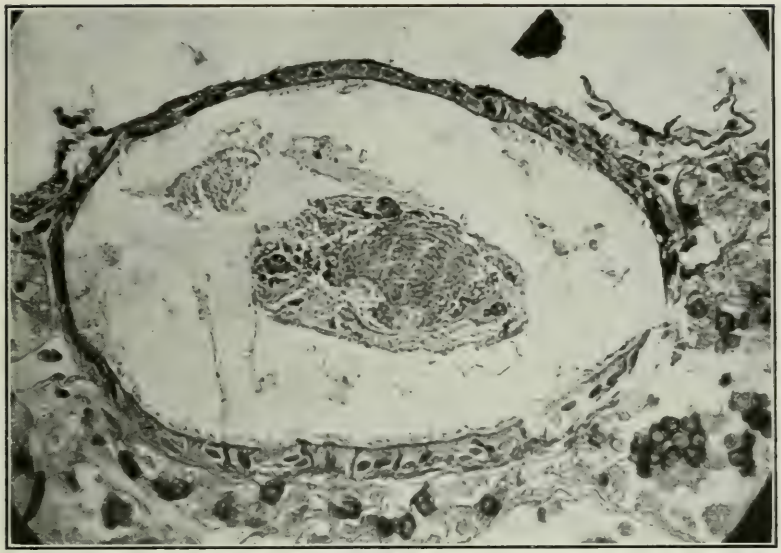


FIG. 4.—A ciliated follicle in extreme anterior portion of the pars anterior.

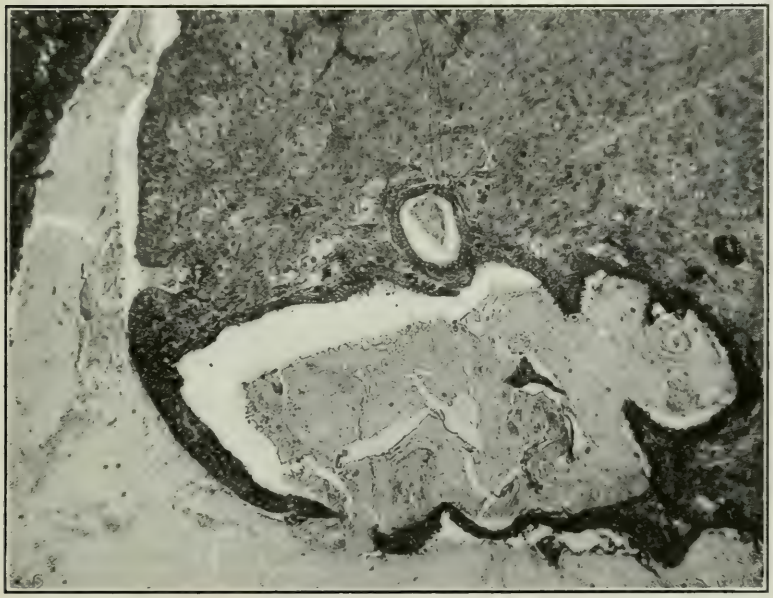


FIG. 5.—Large cyst in pars posterior ruptured through its floor. Secretion faintly basic.

pharynx are not sufficiently differentiated to have the cilia which that region of the pharynx will have later on. It is an inherited potential which these cells, isolated from their original home, eventually demonstrate.

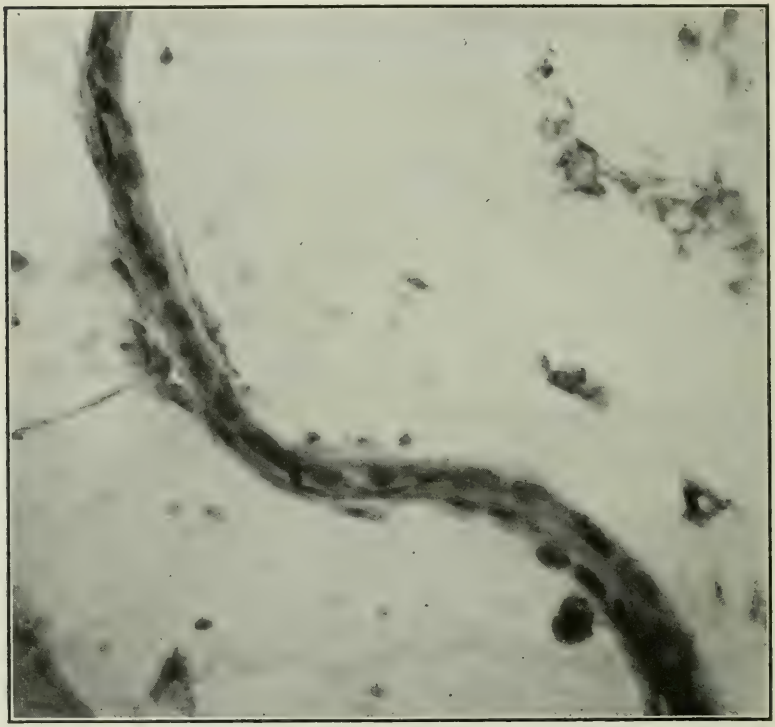


Fig. 6.—Ciliated epithelial lining of cyst in Fig. 5.

At times these globules become quite large. Ziegler speaks of cysts of this type as large as a hen's egg. The next picture (Fig. 5) shows a large globule of secretion, so large in fact that we may term it a cyst. It has ruptured through the pendent part of the pars posterior. The pars anterior is quite flattened. Higher magnification shows that through the substance of the pars posterior in the neighborhood of this cyst there is a greatly

increased amount of secretion. Examining the epithelial lining (Fig. 6) we find a single layer of cuboidal ciliated cells. Now, in the light of the recent finding of globules of secretion in the anterior part of the pars anterior, which globules are surrounded by ciliated cells and are in every way the same morphologically as those found in the pars intermedia and pars posterior, I would

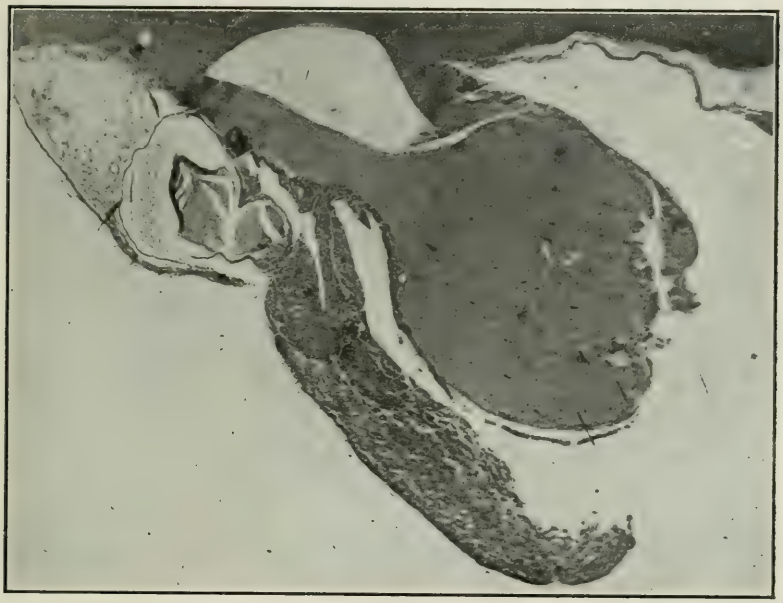


Fig. 7.—A cyst originating in the anterior projection of pars intermedia.

suggest that this function of secretion of what has been thought the specific product of the pars intermedia is a function potentially common to the entire pars anterior. The specimen in question is from a phloridzinized dog. By the appearance of the enlarged pars posterior with its excess of secretion and the flattened pars anterior one might postulate the type of dyspituitarism. In these cystic cases the rapidity of formation of secretion may, by greatly increasing the size of the globules, mechanically impede their

passage through the substance of the pars posterior, and a condition of posterior lobe deficiency might ensue.

The next illustration shows a small cyst of the pars intermedia just above the pars anterior and just posterior and below the optic chiasm (Fig. 7). With higher magnification we find a ciliated lining and fortunately note a drop of secretion about to be discharged into the cyst cavity (Fig. 8).

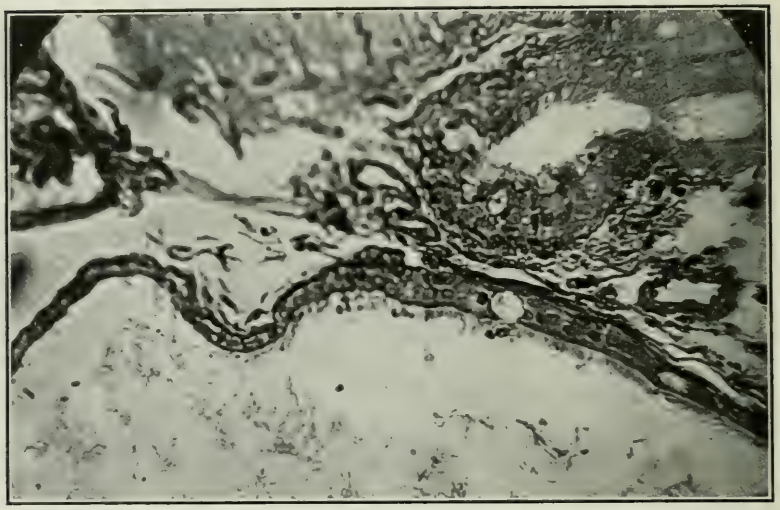


FIG. 8.—A high magnification of the cyst in Fig. 7, showing cilia and a globule of secretion about to be expelled into the lumen of the follicle.

Taking into consideration the fact that a secretion seems to be passed back from the anterior lobe, *via* the pars intermedia into the pars posterior and also realizing the non-parenchymatous appearance of the pars posterior, it occurred to me that possibly the pars posterior might derive its physiological action altogether from the globules of secretion passing through it and that the reason for the difference in action between the pars anterior and the pars posterior was that this secretion in passing through the pars posterior became changed or activated not from anything peculiar to the pars posterior but from some chemical condition common

to nervous tissue in general. If this hypothesis were correct then grinding up in a mortar some of the extreme anterior part of the pars anterior with a portion of brain tissue, let us say from the white matter of the centrum semiovale, and making an extract of this mixture would give a substance which should have the effect of pars posterior and the injection of which would cause glycosuria.

A number of these experiments were performed. The pars anterior used I took from cows and the brain substance from dogs. The animals used for the injection experiments were dogs. In one and only one instance there was sugar which appeared about twenty-five minutes after the injection of the extract. This appeared as a trace rapidly increasing to a heavy reaction with Fehling's solution in about an hour. As a number of following experiments all turned out negative I must conclude that the above premises as stated are incorrect.

In summarizing recent work in the physiology of the pituitary we should better accept the usual division of pars anterior and pars posterior, the latter including the pars intermedia. Removal of one or both lobes in the lower animals and feeding or injection of extracts of one or both lobes have been resorted to in order to determine the physiology of the organ (Fig. 9). This diagrammatic chart represents the consensus of opinion of most investigators (Cushing, Biedl, Schäfer *et al.*). In discussing these actions let us adopt Schäfer's nomenclature. He defines an *autocoid* as a specific substance "produced by the organs of internal secretion for the purpose of either exciting or restraining the activity of distant organs." The exciting autocoids he calls *hormones*, the restraining *chalones*.

Now, concerning glycogenolysis, it is possible that the pars posterior and the intermedia form a hormonic autocoid for the unbinding of liver glycogen, similar in nature to the autocoid of the medulla of the adrenal and opposite in action to the chalone of the pancreas. The glycogen balance may be maintained by the islands of Langerhans on the one hand and the adrenal medulla with the pars posterior on the other. Increase or decrease of the

PARS ANTERIOR.

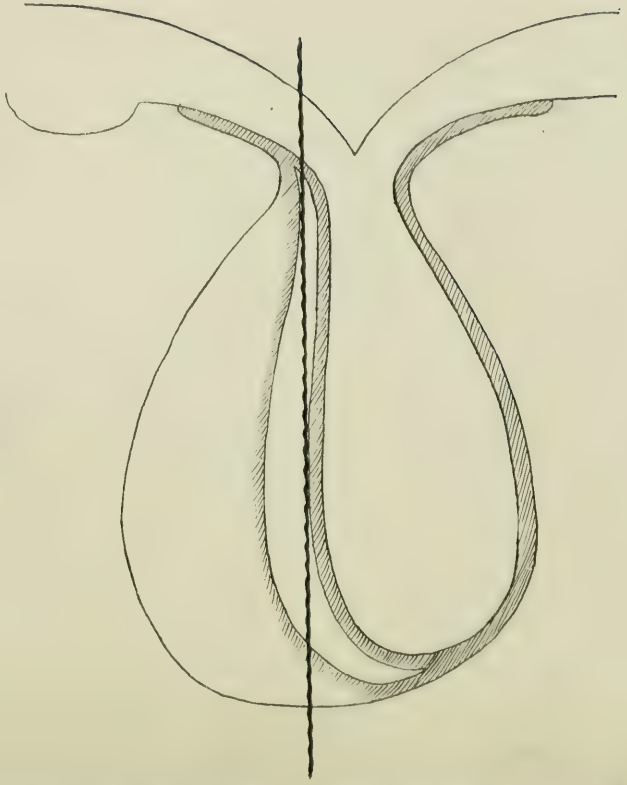
Increased Action.

No definite symptoms.

Decreased Action.

Lowered bodily temperature.

Though no positive experimental demonstration has proved possible. yet it is realized that skeletal development is largely governed by the pars anterior.



PARS POSTERIOR.

Increased Action.

1. Glycogenolysis with glycosuria.
2. Emaciation.
3. Peripheral vasoconstriction.
4. Slowing and strengthening of heart.
5. Increased blood-pressure.
6. Vasodilatation in kidney.
7. Diuresis.
8. Galactogogue (?).
9. Oxytocic (?).

Decreased Action.

1. Increased carbohydrate tolerance.
2. Accumulation of fat.

FIG. 9.—Total removal of pituitary causes cachexia hypophyseopriva: (*a*) muscular weakness; (*b*) subnormal temperature; (*c*) lowered blood-pressure; (*d*) lowered pulse frequence; (*e*) lowered respiratory rate; (*f*) tremors; (*g*) muscle twitching; (*h*) increased reflexes; (*i*) mental apathy, coma; (*j*) polyuria

hormone of the pars posterior disturbs this balance with the resulting glycosuria and emaciation or increased carbohydrate tolerance with fat metamorphosis.

Based on the work of Schäfer it may be said that the only sense in which the pars posterior may be regarded as possessing a hormone for lactation is that it accelerates the emptying of the milk already formed, but there is no evidence that secretion itself is stimulated.

Concerning the oxytoxic action of pars posterior, doubt has recently been cast on the possibility of this action on the virgin uterus. Lieb holds that only in the pregnant uterus is pars posterior active. In other words, the hormone needs an activating substance only present in the pregnant animal. The uterus becomes sensitized to this hormone about six weeks after conception.

The lowered bodily temperature in cases of pars anterior insufficiency has been used by Cushing for diagnostic purposes. Cushing finds that in these cases injection of extract of pars anterior raises the temperature, but in cases where there is no pars anterior insufficiency there is no rise of temperature following the injection.

Turning our attention to the interrelation of the glands of internal secretion we note that there is increased activity in the thyroid following hypophysectomy. There is likewise an increase of the secretion of the pars intermedia in cases of thyroidectomy associated with an increase in the size of the pars anterior. This increase in the size of the pars anterior is due to a hyperplasia of the Hauptzellen. Yet these organs can in no sense replace each other. The secretion of the pars intermedia is also increased on the removal of the pancreas.

In 1912 Dr. Sweet and I studied the effect of hypophysectomy on the testicles. After forty-eight hours a distinct alteration was evident consisting in a failure in completion of the spermatogenetic cycle. After a week there were but few spermatozoa found within the lumen of the seminiferous tubules. By the third week the several types of cells showed marked disintegration with detachment and a collection of cellular detritus in the lumen. In

one of our hypophysectomized dogs we resorted to feeding animal with extract of anterior lobe. The degenerative change in the testicles in this case seemed to have been greatly retarded. Now, it is a fact that removal of the pars posterior in the majority of cases leads to anaphrodisia and testicular atrophy in the male and loss of rutting period in the female, and in puppies to a condition of sexual infantilism. The use of extract of anterior lobe in certain functional cases, the most demanding symptom of which is sexual impotency, is followed by very gratifying results. These three statements at once raise the question whether the specific sexual hormone does not depend on the pars anterior and intermedia and not on the pars posterior. Another point bearing on the possible relation between the testicles and the pars anterior is the fact that after removal of the testicles there is an increase in the eosinophile cells of the pars anterior and a gain in weight in the pars anterior. These observations have been noted in guinea-pigs, rabbits, and steers. Therefore the testicles are in relation with the eosinophiles and the thyroid in relation to the Hauptzellen.

One of the most interesting phenomena is the change in the pars anterior during pregnancy. This consists of a great hyperplasia of the Hauptzellen. At the termination of pregnancy there is a retrogression in the Hauptzellen but never to the condition obtaining in virginity. Each successive pregnancy adds to the number of permanent Hauptzellen to such an extent that some histologists claim to be able to differentiate between a multipara and a primipera or virgin.

In stating the clinical application of knowledge of the physiology of the pituitary to diagnosis I would accentuate the following statement: Rarely does one see a case of pure, unmixed increase or decrease in function of the pars anterior or pars posterior. At times the symptoms are so inextricably mixed that it is difficult to say which type predominates. A case beginning as a typical acromegaly may in the end present the picture of hypopituitarism. A process of hyperplasia and extreme overfunction of one lobe may by virtue of pressure largely or entirely check the function

of the other lobe, giving the picture of hyperpituitarism of the one lobe and hypopituitarism of the other. These mixed syndromes may be designated as dyspituitarism.

Clinically we differentiate four types of pituitary disorder depending, first, on whether we have to do with an increase or decrease of function; second, on whether the patients have been first affected in infancy or adult state. Hyperpituitarism coming on in infancy or before ossification in the epiphyses has taken place gives the picture of gigantism and is known as the *typus Launois*. Hyperpituitarism coming on later in life gives the picture of acromegaly, the *typus Marie*. As we cannot reproduce these pictures by the injection of gland extract we must assume that the hyperpituitarism is more a perverted secretion than an increased normal secretion. Hypopituitarism occurring in infancy or early childhood gives a picture of sexual and skeletal infantilism with marked adiposity and is termed the *typus Fröhlich*. When hypopituitarism occurs in adult life although the skeleton is developed there is a reversion of the sex organs to infantile conditions and a great deposition of fat. This latter type is at times spoken of as *dystrophia adiposogenitalis*.

Concerning acromegaly it may be said that in most if not all cases we have to do with an adenomatous hyperplasia of the eosinophile cells of the pars anterior.

VISUAL PHENOMENA IN PITUITARY BODY DISEASE[1]

By G. E. de SCHWEINITZ, M.D.

That the visual disturbances of pituitary body disease in general, and, for the moment without reference to the type, *i. e.*, whether there is excessive activity of the glandular epithelium (hyperpituitarism), or diminished function of the anterior lobe (hypopituitarism), represent the most common neighborhood signs, as well as the most serious ones, of lesions in the hypophysis is well known. These visual disturbances are, for the most part, dependent on compression of the optic chiasm, optic tracts, and the optic nerves; but, as Cushing[2] has pointed out, the extent of the involvement of the structure bears no direct relation to the size of the sella, *i. e.*, there may be, and often is, a very large sella, for example, in acromegaly, without the slightest evidence of abnormality in the function of sight. The visual phenomena may be catalogued as follows:

1. Impairment of vision, varying from blurred sight to amaurosis or complete blindness.

2. Intra-ocular optic-nerve alterations, varying from partial or general pallor of the nerve head, to partial or complete atrophy; less frequently postneuritic atrophy, and rarely papilledema and non-prominent optic neuritis.

3. Alterations in the visual field for form and colors, concentric contraction, unstable defects, quadrant defects, homonymous and heteronymous hemianopsia and scotomas—central, paracentral and peripheral.

[1] Read March 3, 1915.

[2] The Pituitary Body and its Disorders, p. 243.

4. Other ocular symptoms which have been described are as follows: visual hallucinations; chromatopsia, especially cyanopsia; persistent photophobia; palsy of various exterior ocular muscles; nystagmus; exophthalmos; thickening and pigmentation of the eyelids, with hypertrophy of the palpebral glands.

1. Impairment of Vision. Naturally, degradation of visual acuteness is directly related to the degree of disturbance in the optic paths. Uhthoff's analytical results yield 28.5 per cent. of amblyopia and amaurosis in affections of the hypophysis or the hypophyseal region, without acromegaly or other trophic disturbance, and 7 per cent. with acromegaly or other trophic disturbance, an average, therefore, of 17 per cent. Commenting on these data, Uhthoff[1] says: "The relatively high percentage of amblyopia and amaurosis, without reported details, in hypophysis tumor as compared with acromegaly is partly explained by the fact that in the former case a relatively large number of records date from a period when ophthalmic diagnosis was not carried out, that is, from a period prior to 1886, when Marie demonstrated the nature of acromegaly." He also refers to 10 per cent. of optic-nerve atrophy where compression of the chiasm and optic nerves was anatomically demonstrated; these data, however, come from an early period, and accurate analyses of eye symptoms and ophthalmoscopic appearances are lacking. Therefore, as he states, it is most important to make accurate investigation of ocular signs and of the nature of their earliest manifestations, especially as hypophysis affections may begin early in life, progress very slowly, and long periods of time may elapse before serious visual symptoms develop.

With these facts in mind, I desire first to call again particular attention[2] to a form of blurred vision, of which the patient is definitely conscious, which antedates by a long period of time the amblyopia which is associated with ophthalmoscopic nerve-head changes, or any form of scotoma, or any visual field defect (searched for by the usual methods), or any failure to read nor-

[1] Trans. Oph. Soc. U. K., 1914, xxiv, Bowman Lecture.
[2] Jour. Amer. Med. Assn., September 12, 1912, p. 1041.

mally the ordinary test types. This period of time may last for months, even for years: in one patient it continued for almost two years before change in the color of the disk was noticeable. Doubtless careful estimation of the light sense would reveal that it is deficient, just as it is in chronic glaucoma long before the conspicuous symptoms of the disease are present. It is a symptom difficult to describe. In an attempt at description one patient expressed herself thus: "Yes, I can see and read the letters which I ought to see and read, but I see them as if I was in a brown study." How frequent this phenomenon is I do not know; it readily may escape detection. I have observed four notable examples of it. It may be unilateral. Evidently it interprets a beginning physiological block to light impulses; indeed, the later primary atrophy of the optic nerves represents a more or less complete similar block, and not a destruction of the nerve fibers in those patients whose sight is restored by operation or organotherapy. The importance of further study of this condition is evident.

2. Intra-ocular Optic-nerve Alterations. Visual disturbances are much more frequent in patients with primary hypopituitarism than in acromegalics, and in the majority of cases of hypophysis tumor with visual field defects (hemianopsia, etc.) the ophthalmoscopic appearances, if they are not negative, are those of so-called simple atrophy, *i. e.*, partial or complete atrophic discoloration of the disks. Indeed, if the affection has existed for a considerable time they are seldom absent (Uhthoff, loc. cit.). Choked disk is recorded by Uhthoff in 9 per cent. of his collected cases and optic neuritis in about the same proportion. I have never seen choked disk but once in my own experience and in the service of various colleagues, chiefly those of Drs. Frazier, Mills, Spiller, and Dercum, and never but once have been definitely sure that I have noticed a postneuritic atrophy. In the late stages, as Cushing points out, increase in the size of the tumor may cause increase in general cerebral pressure, with resulting hydrops of the ventricles and therefore disk edema, which may be implanted upon an atrophic nerve. This I have observed once

As we all know, internal hydrocephalus may give rise to symptoms closely simulating those of pituitary body disease. If the tumor mass surrounds and constricts the nerves, their sheaths cannot be distended by the cerebrospinal fluid, and edema does not take place. This point is made both by Cushing and Uhthoff.

It is an important and an interesting fact that the so-called simple atrophy of the optic nerves, associated with tumors of the hypophysis, may present all the ophthalmoscopic appearances of completeness, and yet marked improvement in vision may follow a successful operation or prolonged organotherapy. I have studied one patient and recorded her case history,[1] whose optic nerves were to all appearances totally atrophic, with absence of light perception lasting twelve days in the right eye and six weeks in the left, who regained normal vision in each eye after several months of almost constant exhibition of large doses of thyroid extract, and who is perfectly well at the present time, and capable of doing the arduous work of a school-teacher. Marked visual improvement I have observed in several patients within a very short time after sellar decompression performed by Drs. Frazier and Landon. In one patient the vision rose in the left eye in a few weeks from one-third of normal to the full normal standard; the right eye, blind at the time of operation, remained blind. In these patients evidently the light impulses were blocked, but the nerve fibers, certainly not all of them, were not degenerated. Recently, I have studied some sections of optic nerves in Dr. Cushing's laboratory, stained according to the Weigert and Weigert-Pal method, and was more than astonished to find comparatively little degeneration, although ophthalmoscopically the nerves had been partly atrophic and the visual field hemianopic. While prognosis must always be guarded it would be very wrong to advise against operation or treatment because the nerve had the appearance of atrophy and the vision was lost or greatly degraded.

Bogatsch[2] has investigated the material of the Breslau Clinic

[1] Pennsylvania Medical Journal, April, 1912.
[2] Klin. Monatsbl. f. Augenheilk., 1912, Bd. xiv, p. 313.

in order to determine the frequency of an affection of the hypophysis in the presence of bitemporal hemianopsia—that is, the material for the last ten years—and found that over 50 per cent. of the cases had a lesion, presumably a growth, in the hypophysis or its vicinity. Indeed, if the cases are included in which an affection of the hypophysis could not be excluded the percentage is considerably higher than this. In point of fact, in only 5 of the cases analyzed, 34 in all, was it possible to demonstrate that the hypophysis was not affected; in 19 it certainly was, in 4 it probably was, and in 6 the etiological factor was not determined. Therefore it is not strange, again to quote Uhthoff, that we constantly meet with this sentence in the literature: "The most typical and most characteristic visual disturbance in affections of the hypophysis is undoubtedly heteronymous bitemporal hemianopsia, a condition which has been observed in about 40 per cent. of patients with hypophysis tumors and diseases of the infundibulum, with and without acromegaly." It is usually stated that this form of hemianopsia is more frequently observed in hypophysis affections with acromegaly than in those without trophic disturbance in the proportion of 50 to 30 per cent. and often stated that the boundary line is vertical. And yet it must be the experience of everyone who has investigated many patients with pituitary body disease:

1. That in spite of what the books say the boundary line is hardly ever regular or vertical. In Cushing's series typical bitemporal hemianopsia with a vertical meridian which bisects the macula was conspicuously rare, a statement which is confirmed by Evans in his well-known article, and certainly I have rarely seen it in the many fields which have been charted by myself and by members of my staff. It must not be inferred from what I have said in regard to the sharpness of the boundary between the seeing and the blind field that a typical vertical meridian which bisects the macula does not occur. It is only that one does not often have the opportunity of making the examination when, to use a modern expression, "the field lingers" with this shape for a long period of time.

2. Although it is true that homonymous hemianopsia due to an optic tract lesion is less common than bitemporal hemianopsia, I doubt if it is fair to say that it is very rare in hypophysis tumor, as Uhthoff maintains. Certainly, it is not very rare if with homonymous defects we include what Cushing calls the tendencies in this direction, and with this inclusion he makes them at least half as frequent as bitemporal ones. I have seen recently 2 cases of homonymous hemianopsia with pituitary body disease, 1 submitted to operation with marked benefit, and have in previous years observed several others, 2 with acromegaly, which have been placed upon record. It is an important point, because if not dwelt upon, or well understood, by those who have the opportunity of investigating patients with ocular disturbances the presence of a homonymous defect in the visual field might turn attention away from the hypophyseal region when, in point of fact, it ought to be focussed there.

In patients with homonymous visual-field defects atrophic discoloration of the disks may be expected, and, indeed, this discoloration may progress until the appearance of complete atrophy is present and blindness results, preceded by a gradual reduction of the retained halves of the visual field. If the reduction of the remaining halves is a symmetrical one it is fair to assume that the second optic tract is gradually being pressed upon. If, on the other hand, the pressure of a tumor upon one tract spreads in such wise that it presses upon the chiasm the reduction of the remaining fields is not symmetrical. Attention to these points, as has been pointed out by a number of observers, renders it possible to make a reasonably exact basal localization.

3. In all cases the defect for colors precedes that for form. The involvement of the form field is a later development. This is a very important matter, and it is important also that the color field shall be mapped with all of the usually selected primary colors—that is, blue, red, green—because, for example, the color defect may at first be present only with one of these primary colors, for example, green. This was conspicuously the case in one of my own patients, where a partial green hemiachromatopsia

was present for a long period of time before red and blue were affected, and they in turn preceded the defect of the form field by a number of months.

Unilateral hemianopsia may be caused by a pressure more pronounced upon one nerve than the other, and so it may come about that there is a unilateral blindness, with very little disturbance of the boundaries of the visual field upon the opposite side, although I suspect that in some of these cases, that is to say of preserved visual field upon one side with blindness upon the other, if the newer methods of taking the visual field had been diligently practised, some of the earlier characteristics of the field would have been noted.

Referring now particularly to the types of visual field disturbance which terminate in bitemporal hemianopsia, it may be said that in the large majority of the cases it will be found that the temporal field tends to be lost from above downward, although as Fisher, who was, I think, one of the first, if not the first, observer to point out this fact, states, this is not an invariable rule. This so-called "temporal slant" begins first with colors and afterward is found in the form field. I shall presently demonstrate in a series of charts the progression of the visual field defect, beginning in this wise and going on to total loss of vision. It must be remembered that even in the presence of total blindness, or practically total blindness in the one eye, one would be justified in assuming that primarily there had been a bitemporal hemianopsia, not only if the defect in the still seeing eye has a sharply defined vertical boundary line, but because it is almost always possible, unless the blindness is absolute, to detect with a small point of electric light some area of sensitiveness in the visual field. Thus, in a recent case examined with a temporal hemianopsia of one eye and practical blindness in the other eye, a light held in the temporal half of the blind field was totally undetected, but almost invariably the patient stated, when the test-light was carefully passed over to the nasal side (of course without her ability to observe the maneuver), "it seems brighter." Sometimes a small sensitive area is found in one eye, the other

eye being totally blind, which is reasonably sharply isolated, and which can occasionally be detected only with a very small point of electric light.

4. A matter of some importance, which has been dwelt upon by a number of authors, but notably insisted upon by A. de Kleijn,[1] is the variations which the visual fields in pituitary body disease undergo. If daily or even more frequent perimetric examinations are made, a classical hemianopsia may be present at one time, but later it will be found that it has given place to an ordinary concentric contraction. Or the reverse is true; there may be a concentric contraction, due, doubtless, to pressure upon the peripheral optic-nerve fibers, which may even go on to temporary practical total loss of vision, and when the visual field reappears, a bitemporal hemianopsia can be demonstrated. A case of this character has been placed upon record by Uhthoff. De Kleijn refers to the so-called insular-shaped fields in hypophysis disease, these islands being subject to variations, not only in their number but also in relation to the part of the visual field which they occupy. These peculiarities in the perimetric examination doubtless depend upon the varying degrees of pressure of vascular and cystic growths in this region. Figs. 1 to 8.

5. I now come to refer to the important relationship of scotomas to this disease. Long ago, Mr. Nettleship, discussing central amblyopia as an early symptom in tumor of the chiasm, referred to certain types of scotoma which resembled those produced by toxic agents, and found in one instance that the chiasm was incorporated in the front wall of the cyst. In all cases of suspected pituitary body disease, careful search for scotomas must be made, especially as these scotomas may in a later stage develop into various types of bitemporal hemianopsia. Just because the alterations in the visual field are subject to marked variations, it is difficult to arrange a classification of these scotomas. Dr. Holloway and myself, who have worked at this matter with some

[1] Archiv f. Ophth., 1911, lxxx, Part 2, p. 307.

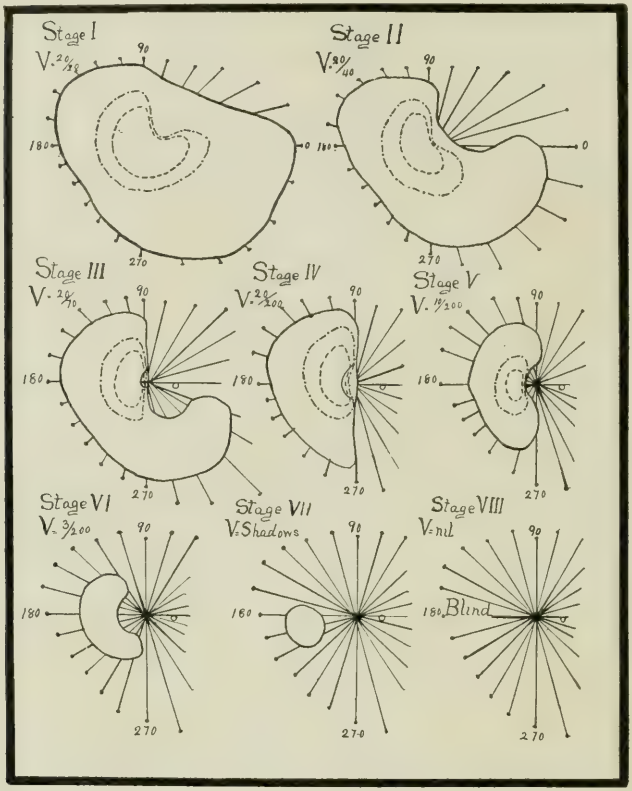


FIG. 1.—Gradual development of temporal hemianopsia and its progression to complete blindness. From a slide prepared by Dr. Harvey Cushing, and utilized with his permission.

Before operation.

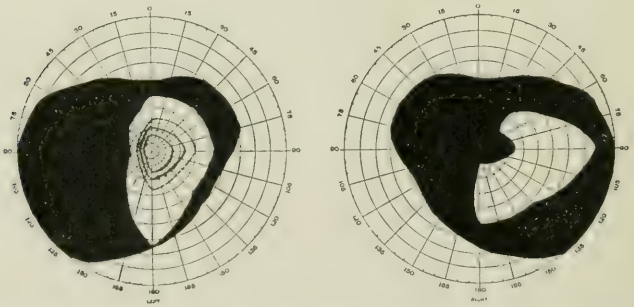


FIG. 2.—Pituitary body tumor and left lateral hemianopsia, with loss of macular area of right eye. Before operation.

degree of faithfulness, have made the following attempt in this respect, and I now quote from a previous paper on the subject.

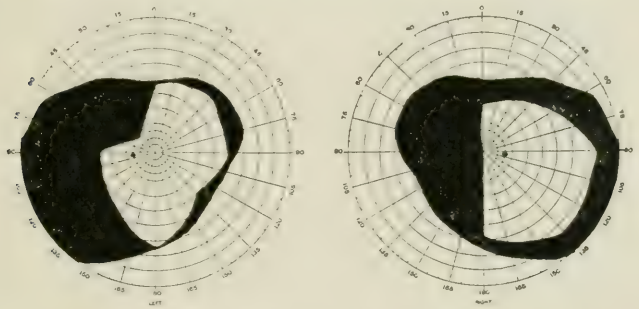


FIG. 3.—Visual fields one month after sellar decompression by Drs. Frazier and Landon, showing restoration of lost central area of right eye and beginning return of field from below of left eye. Same case as illustrated in Fig. 2.

Before operation.

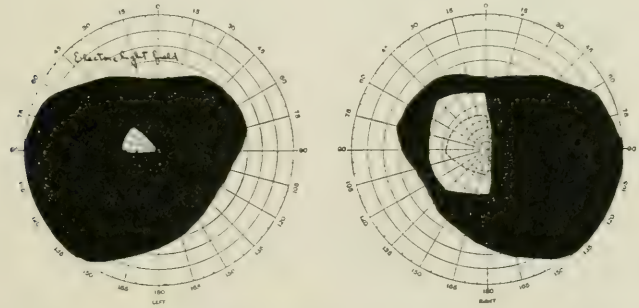


FIG. 4.—Tumor of pituitary body. Before operation. Right lateral hemianopsia. Note the small preserved field on the temporal side O.S. No red or green sense O.D.

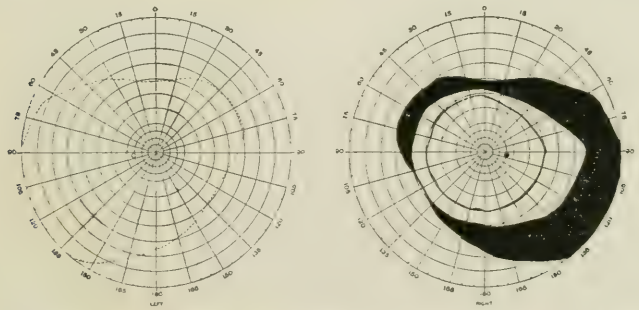


FIG. 5.—From same patient whose fields are depicted in Fig. 4. One month after sellar decompression, by Drs. Frazier and Landon. Compare with Fig. 4. No change in left field.

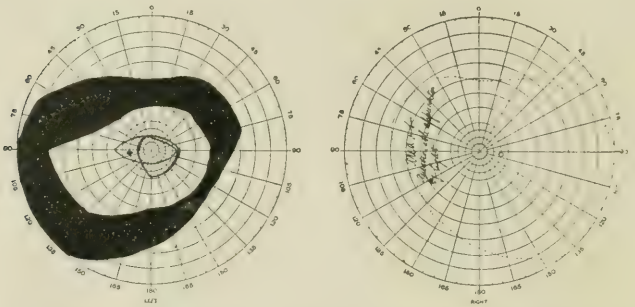


FIG. 6.—Pituitary body struma. Right eye blind except questionable area of light-sense in nasal field. Note temporal slant in contracting field of left eye.

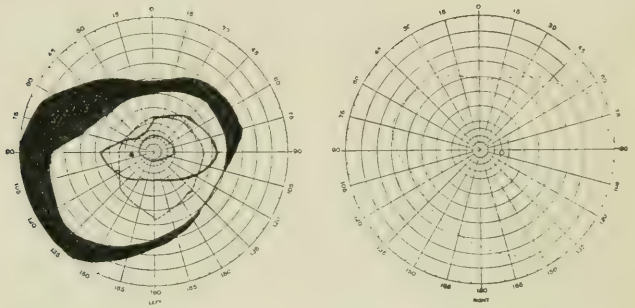


FIG. 7.—Left field of patient whose field before operation is noted in Fig. 6. One month after operation. Note enlargement of the field, especially from below, and increase in the size of color fields, with restoration of the blue sense previously lost.

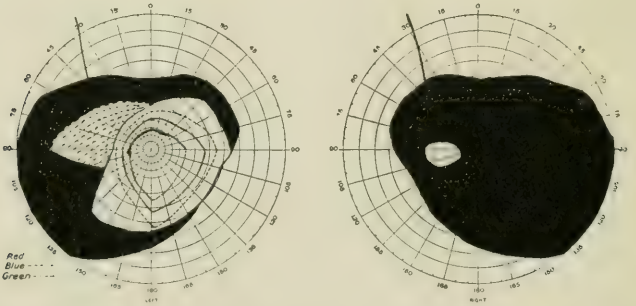


FIG. 8.—Pituitary body struma. Right eye blind except small area in nasal field in which electric light is uncertainly seen. Partial left hemianopsia, O.S., with marked temporal slant capped by an area of imperfect perception of light.

1. These scotomas may be small and paracentral. Subsequently, with increase in the size of the growth and of the pressure symptoms, they may expand into complete hemianopsia. There may be,

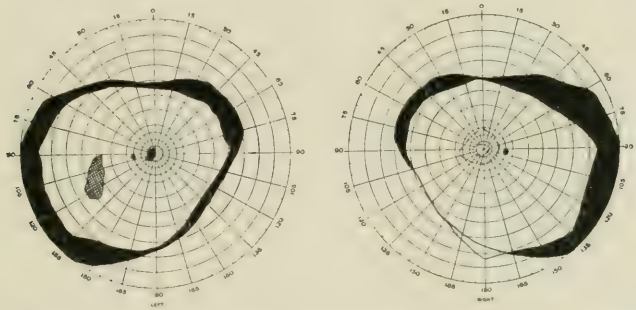


FIG. 9.—Author's case; pituitary body tumor. Small absolute paracentra (hemianopic) scotoma in left field and larger scotoma in left temporal field. Concentric contraction. Later complete bitemporal hemianopsia, and still later complete blindness. Ultimately perfect recovery of vision and field of vision as result of exhibition of thyroid extract.

as, for example, was the case in Marlow's[1] patient with hypophysis disease, in one field a scotoma just outside of the fixing-point and a larger one, more produced to the temporal side but including

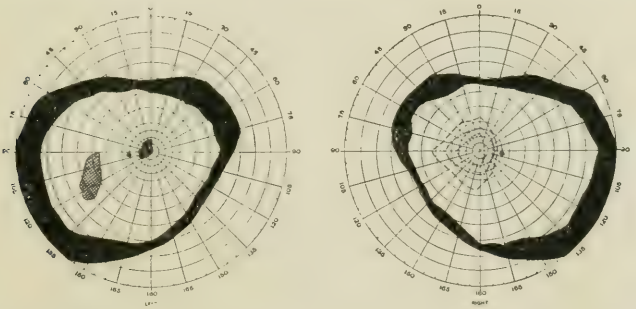


FIG. 10.—Another chart of visual fields. Compare with Fig. 9. Scotomas as previously noted; color defective in right field; almost complete loss on temporal side.

the fixing-point, in the opposite field (Fig. 13), the peripheral fields at the same time being comparatively full. Or there may be, as

[1] New York Med. Jour., 1910, xci, 794.

in one of our own cases, a small paracentral scotoma of one field, with a contraction of the color field of the opposite eye, the

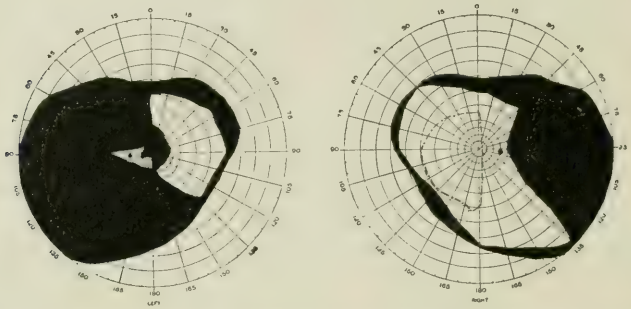


FIG. 11.—Later stage of fields shown in Figs. 9 and 11. Scotoma in left field enlarging and encroaching on nasal side; almost complete loss of temporal field; complete temporal loss of colors in right field and partial temporal loss of form field.

contraction being relatively greater on the temporal side (compare Figs. 9 and 10).

2. An absolute or relative defect may be detected up and out, forming a quadrant. Such scotomas may be bilateral or sym-

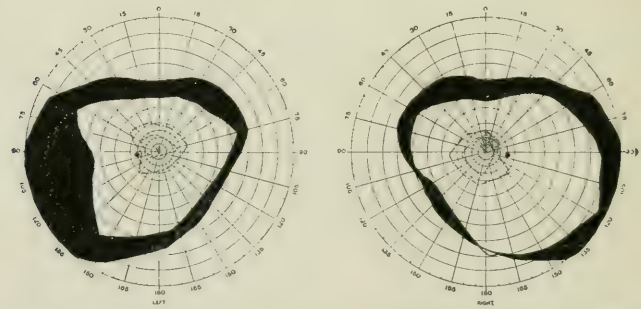


FIG. 12.—Visual fields from same patient whose fields are shown in Figs. 9, 10, and 11, after beginning improvement from organotherapy. Hemianopsia has disappeared; concentric contraction remains; scotoma up and out for colors in right field and central in left field.

metrical, or nearly so, the larger scotoma, however, usually being seen in the field of the eye with the poorer vision, or the scotoma

may be unilateral (Fig. 14). A somewhat similar instance, the left scotoma being directly above the fixing-point and the right one up and out in the usual position, has occurred in our own

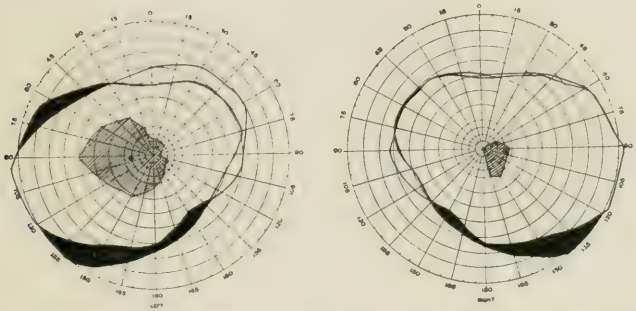


FIG. 13.—Marlow's case of acromegaly with large temporal scotoma, somewhat resembling bitemporal defects described by Uhthoff as suggestive of pituitary body tumors.

experience (compare Fig. 17). Again, the scotoma may exist in one field in the position previously named and be associated with a small central scotoma in the opposite field, as in one of our own

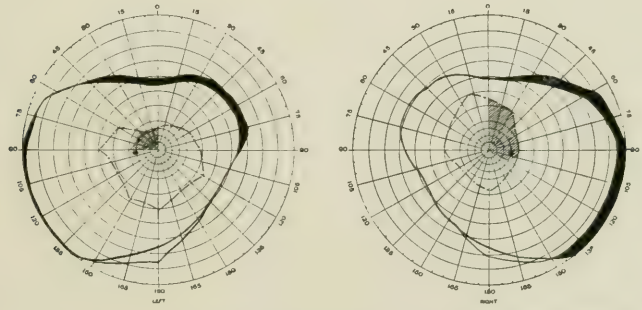


FIG. 14.—Doyne's case of acromegaly; scotoma up and out from fixing-point; later bitemporal hemianopsia.

patients during the period of convalescence from pituitary body disease (compare Fig. 12).

3. Just as the visual fields in vascular basal disease, particularly if the hypophysis is involved, may vary from day to day, certainly

from week to week, owing to the varying degrees of pressure which the neoplasm or struma produces, so it is possible that these scotomas vary in size and in position, and that they may be

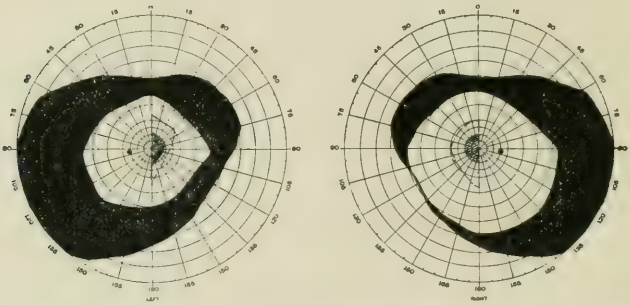


FIG. 15.—Binasal scotoma, lasting two weeks; bitemporal color defects. Zentmayer's case of acromegaly.

present for a period of time and then disappear. For example, in Zentmayer's[1] well-reported case hemianopic scotomas persisted for two weeks, and, moreover, on the nasal side, and were associated with contracted form fields and with bitemporal hemianopic

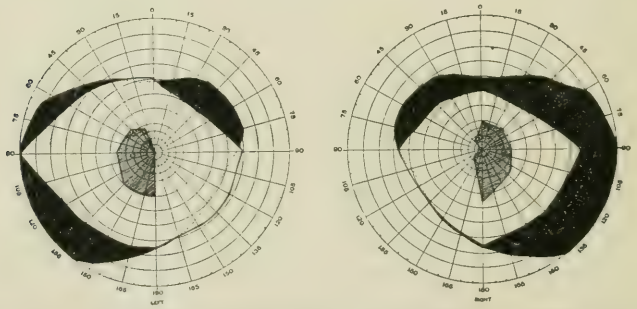


FIG. 16.—Visual fields of Pontoppidan's patient with large bitemporal hemianopic scotomas.

color defects (Fig. 15). Curiously enough, it may happen that after more or less typical visual-field defects have disappeared as

[1] Ann. Ophth., 1910, xix, 719.

the result of treatment, a recrudescence of visual disturbances may arise, dependent on the presence of large central scotomas. Another variation is contracted form field, color hemianopsia and

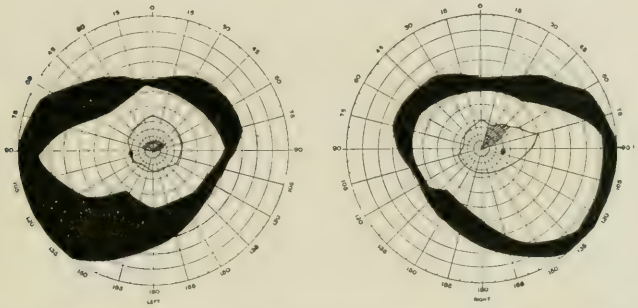


FIG. 17.—Author's case; pituitary body tumor. Concentric contraction; scotoma up and out from fixing-point in right field and above fixing-point in left.

central scotoma, as, for example, in Kocher's[1] patient, diagnosis having been settled by operation. Again, as in Bartels'[2] case, there may be contraction of the form and color fields and central relative scotomas.

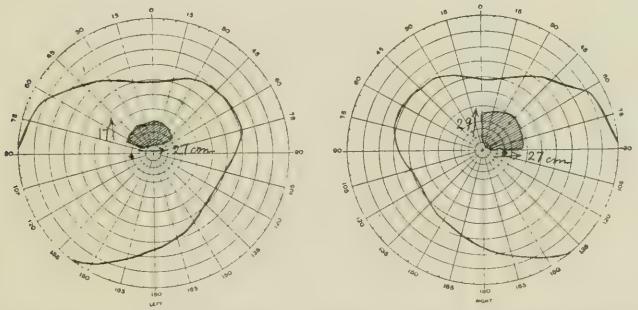


FIG. 18.—Same scotomas as in Fig. 17, charted on a black screen at one meter's distance from patient's eye with a 3 mm. white object.

4. Kund Pontoppidan[3] has observed with normal form fields large bitemporal hemianopic scotomas, absolute in the right

[1] Deutsch. Ztschr. f. Chir., 1909, c, 13.
[2] Ztschr. f. Augenh., 1906, xvi, 407.
[3] Hospitalstid., December, 1897, xl, 1137.

field and relative in the left, due to a tumor situated within the circle of Willis, extending from the anterior border of the pons to the chiasm. The infundibulum emerged from the most prominent portion of the growth (Fig. 16). Uhthoff[1] has demonstrated and insisted that such large paracentral absolute scotomas in the outer halves of the visual field are a conspicuous and, according to his observations, a frequently observed phenomenon in connection with hypophysis tumors.

5. Occasionally a scotoma has been noted in the temporal field at some distance from the fixation-point which is manifest before, and, in point of fact, at some considerable time before, the entire field is obliterated. This we have observed in one undoubted case of pituitary body disease and in another case supposed at the time to be of like nature, but in which subsequently an autopsy demonstrated that the pituitary body itself was uninvolved in a neoplasm, but probably that the pressure was on the tract posterior to the chiasm. In the field of the first of these patients the scotoma existed as an oblong area lying below the horizontal meridian which it touched at its upper end, and therefore it was in the lower and outer quadrant of the field. In the same field there was a paracentral scotoma of the type already described (compare Fig. 10). A very similar visual-field defect which occurred in the second case (the pressure in this instance having been on the tract, so that ultimately a homonymous hemianopsia developed), occupied an exactly similar place, although it was not so great in extent, and, moreover, was in a field which was not subsequently obliterated. Nothing in the eye-ground accounted for the presence of these scotomas, and their explanation is not very clear. They are mentioned here not because they seem to have any very great significance—at least the observations are too limited in number to place any satisfactory interpretation on this visual-field defect—but rather because they belong to what may be described as some of the curiosities of the visual-field phenomena in basal disease of the

[1] Klin. Monatsbl. f. Augenh., 1911, xlix, 393.

brain. It is not uncommon to find islands of preserved vision in the dark fields of pituitary body affections which have a similar appearance. These islands have somewhat the same situation and extent which these scotomas present. In other words, in the one instance an area is preserved which in the other is obliterated.

It would be interesting, taking Wilbrand and Saenger's[1] plan of the distribution of the fibers in the optic chiasm as a guide, to attempt to place the probable situation of the lesion which these scotomas interpret, but in large measure such an attempt would be a piece of guesswork, except in a few instances. Thus, in all probability bitemporal hemianopic scotomas could be explained by assuming that a circumscribed focus of disease proceeding from the floor of the recesses to the surface of the posterior portion of the chiasm, meets the crossed fibers of the papillomacular bundle and produces this visual-field defect. On the other hand, should the lesion extend symmetrically on both sides of the posterior upper surface of the chiasm, the uncrossed fibers of the papillomacular bundle would be affected and binasal hemianopic scotomas would result (see Fig. 15). Scotomas such as are charted in Fig. 14 may perhaps be regarded as the initial stage of the visual-field defect which later is elaborated into a large bitemporal hemianopic scotoma, and ultimately into a complete bitemporal hemianopsia. Apparently the lesion would, in these instances, first involve the crossed bundle and the crossed papillomacular bundle in their inferior portion. As Bartels points out, it may happen that although the visual disturbances may depend on the presence of a central scotoma, no clear explanation for its presence is demonstrable at autopsy.

There seems very little doubt that some of the visual-field defects caused by basal disease depend on vascular constriction.

A few words may be said in regard to the remaining ocular symptoms of pituitary body disease. At one time, following the teaching of Henschen, it was assumed that visual hallucinations occurring in focal brain disease indicated the position of the lesion

[1] Die Neurologie des Auges, 1904, iii, 110.

to be in the occipital lobe. Dercum and myself, however, have shown that they can be present in the form of homonymous hemianopic hallucinations with disease of the right optic tract, proved by autopsy, and Uhthoff records 0.8 per cent. of visual hallucinations in his investigations of pituitary body phenomena. I have myself never observed the condition in a pure pituitary body case, although I know of no reason why the phenomenon should not be evident if pressure was exerted on either of the optic tracts, as it was in the patient to whom I have just made reference. These hallucinations may occur on the blind side of the field only, or may precede the hemianopsia. Chromatopsia in the sense of blue vision, or cyanopsia, noted by Evans, I have myself not seen, nor is it referred to by Uhthoff. Persistent photophobia, especially after operative interference, has been noted a few times, once, if I am not mistaken, by Holloway. Depending upon the character and condition of the pressure, there may be naturally palsies of the various ocular muscles, for example, complete oculomotor palsy, as in one of my own patients, or abducens palsy, or palsy of the superior oblique, which I have once seen, or occasionally, as Uhthoff has reported, a complete ophthalmoplegia externa. Not enough patients have been examined by the careful methods which are now in vogue, especially by the instrument of Hertel, to determine the frequency of exophthalmos; but I know of no reason why in the later stages, particularly in large pituitary body growths, it should not be a prominent symptom. Uhthoff refers to it as a comparatively rare manifestation. It is probably always a pure stasis phenomenon. To pigmentation of the lids the difficulty of eversion of the lid, the thickening of the palpebral glands, and nystagmus, occasional reference will be found in the reported cases. The pupil phenomena will depend upon the pressure, and the hemianopic pupillary inaction has been found in cases of hemianopsia of the bitemporal variety.

In closing, I would like to say one word in regard to the restoration of the visual field, some examples of which I shall presently show. In the first place, the two eyes are rarely affected to an equal degree, and it is probable that very careful examinations

will show that frequently the restoration is in a reverse order. Indeed, many of the defects in the visual field, which are now being studied with such great care, especially with very small test objects, such as Walker has designed, and by the Bjerrum method, seem to indicate that the lines of the visual field restore themselves from below upward in a series of what I presume I may call sloping curves. Time does not permit me to go into this matter with any great detail, nor have I any diagrams to show it accurately. Some very elaborate studies in this respect have been published by Harvey Cushing and C. B. Walker.[1] Infinite pains are required in testing the fields, and either the test objects recommended by Walker, or similar test objects, such as many of us have seen originally placed upon the market by Sydow, are very important. This much may be said, that accurate perimetric work cannot be done with an automatic registering perimeter. This we all know from personal experience and from the condemnation which it has received from Wilbrand, Rönne, Semon, and more recently from Walker and Traquair. With Duane's screen the field can be admirably mapped, although it is a somewhat tedious process to make the record.

[1] Brain, March, 1915, xxxvii, 341.

CLINICAL MANIFESTATIONS OF PITUITARY DISORDERS IN THEIR RELATION TO SURGERY[1]

By CHARLES H. FRAZIER, M.D.

The most striking feature of the pituitary body is the multifarious ways in which disorders of function express themselves. On the one hand, there may be the picture of a full-fledged acromegaly; on the other, perhaps nothing but a suggestion of hypersecretion. It may be said, without fear of contradiction, that no other gland of the body, with or without a duct, has so baffled both physiologist and clinician in an attempt to straighten out the tangle of the true function of the respective glandular elements in health, and of their perverted function in disease.

In the years which have elapsed since the perversions of the thyroid gland first became the subject of much study, the disorders of this gland have fallen pretty generally into two categories—those of hyperactivity or hyperthyroidism, and those of diminished secretion or hypothyroidism. During the first years of our intensive study of the pituitary body, there seemed to be a striking analogy between the two glands, in that the disorders of each fell into one of two groups—one the result of hyperfunction, and the other of hypofunction. The thyroid gland in its pathological cycle sometimes passes from a state of hyperplasia to one of hypoplasia; so also hyperpituitarism may give way in time to hypopituitarism. But the pituitary body has this striking, distinguishing feature, namely, that in the same subject will be found in combination evidence of both hyper- and hypofunc-

[1] Read March 3, 1915.

tion. A classification of the medley of symptoms into sharply defined, clinical groups must, for the time being, be abandoned, and we must content ourselves in most cases with the use of the term dyspituitarism for all cases not strictly conforming to the acromegalic or Fröhlich type.

In the hypophysis we are dealing not only with a bilobed gland, but with a gland in which the two lobes are anatomically and physiologically quite different. While it happens, of course, that in certain cases both lobes have become atrophied or hypertrophied, it is also true that a primary hypertrophy with hypersecretion in one lobe—most frequently the anterior—may so compress the posterior lobe as to diminish its activity. If, in the normal, the function of the two lobes are utterly different, what complications and difficulties arise when the function of each is disturbed! The complexity of the picture and the difficulty of its interpretation is further increased by the fact that it is often impossible to differentiate between intra- and extrasellar lesions. A primarily intrapituitary lesion frequently causes extrapituitary symptoms, neighborhood symptoms and the like; while an essentially extrasellar and extrapituitary tumor, through pressure upon the pituitary, may give rise to any or all of the symptoms of pituitary derangement.

Furthermore, is not the hypophysis a link in the chain of internal secreting glands? Witness the emaciation in dyspituitarism of adrenal origin, the occasional signs of hyperthyroidism from involvement of the thyroid gland, the amenorrhea, and the sexual apathy! And the reverse of this is equally true—disorders elsewhere in the chain may in time upset the function of the pituitary.

For convenience's sake the clinical signs of pituitary disorders are assembled in four groups:

Group I. The signs of intracranial pressure.

Group II. The signs of pressure upon adjacent structures.

Group III. The signs of disturbed pituitary function.

Group IV. The signs of polyglandular derangement.

There is in the first group, the symptoms common to brain

tumors of other origin, the headache, the vomiting and the optic atrophy; in the second group there are the sellar deformations, the characteristic bitemporal hemianopsia, first for color and then for form, and the signs of pressure on adjacent structures, as of the uncinate region, and occasionally photophobia. In group four there are the varied manifestations of derangement of other glands, it may be the pineal, the thyroid, the adrenal, the pancreas.

The strictly functional disturbances of the pituitary are not always easy of interpretation. As I have said before, in human pathology, we are dealing most frequently with the complex picture of *dyspituitarism*, since there are few cases of pure hypo- or pure hyperpituitarism. Many complexities arise from the fact that not infrequently symptoms of glandular insufficiency follow close on those of oversufficiency. Moreover, the disturbance of function may be only of one lobe, or there may be hyperactivity in one lobe simultaneous with insufficiency in the other. Thus, it is not strange that we are still unable to forecast correctly the exact nature and location of the lesions.

The hypophysis has very distinct and important functions in that chain of ductless glands which together control skeletal development, metabolism, and sexual life. It is now pretty generally conceded that the anterior lobe has a profound influence over the growth of the skeleton and cuticular tissues, while the posterior lobe and pars intermedia influence carbohydrate metabolism and the contractibility of muscular tissue, particularly of the heart, kidneys, and mammary glands.

The depressing influence of pituitary disease upon the sexual function may be but an expression of that general law in genetics that all useless extremes and mutations, whether on the side of excess or of defect, bring with them the means of their own automatic extinction. Sterility is common to many incapacitating diseases; indeed, it is a well-known biological fact, that the marked decline of any important organ tends not only toward individual, but even toward racial, death as well. But we must await the results of still further research before we can assert with any degree of certainty which portion of the gland is responsible for

the genital atrophy, either of acromegaly or dystrophy. In fact, we cannot be certain that it is to be attributed to a pituitary lesion at all. Certain it is, that after we have removed a pituitary tumor and resorted to glandular feeding, the sexual function has been reëstablished.

At this juncture it is difficult to improve upon Peritz's[1] classification of diseases of the hypophysis, although we must bear in mind that there are many combinations and variations, one symptom-complex frequently being superimposed upon another. Peritz's classification is as follows:

1. Diseases of the anterior lobe:
   (*a*) Hypofunction—dwarfism.
   (*b*) Hyperfunction—acromegaly, gigantism.
2. Diseases of the posterior lobe:
   (*a*) Decreased function—hypophysial adiposity.
   (*b*) Hyperfunction—diabetes insipidus.
3. Mixed forms (acromegaly and adiposity, dwarfism and adiposity).
4. Diseases of the hypophysis in combination with disease of the other glands.
   (*a*) Genital glands and hypophysis—eunuchoidism.
   (*b*) All glands—Claude and Cougerot's pluriglandular disease and Falta's multiple sclerosis.

While observers are not in entire accord as to the precise seat and nature of the lesion in acromegaly, I think we can discard Marie's theory of diminished activity and attribute it to a functional hyperplasia, probably of the pars anterior. It may be a pure hypertrophy or an adenomatous hyperplasia, but usually not a destructive tumor or a hypoplasia, except in those cases in which hyperfunction has passed into a state of hypofunction.

Fröhlich's disease, or dystrophia adiposogenitalis, is unquestionably due to hypophysial insufficiency and is characterized primarily by the clinical triad of trophic disturbances—in the form of adiposity and genital hypoplasia, alterations in the contour of the sella, and the ocular disturbances (bitemporal hem-

[1] Handbuch d. Neurol. 1913, iv, 283.

ianopsia). The skeletal changes, arrest of development, spontaneous fractures, and coxa vara I have not observed in any of my cases. The symptoms accompanying posterior lobe insufficiency—somnolence, slow pulse and respiration, subnormal temperature, low blood-pressure, and a tendency toward adiposity have been characterized as similar to conditions observed in hibernation. While the symptoms accompanying insufficiency of the posterior lobe are pretty clearly outlined, the same cannot be said of those accompanying hyperplasia, except perhaps the frequent occurrence of diabetes insipidus. It is quite possible that just as obesity results from a hyposecretion of this lobe, so emaciation may accompany a hypersecretion. Experiments with posterior lobe extracts would seem to bear out this supposition. It is true, at any rate, that a certain percentage of dwarfed pituitary cases are very much under, rather than over, weight.

The more one sees of the clinical side of pituitary disorders, the more one is struck with frequent departures from the conventional types, such as acromegalic and the Fröhlich syndrome: (1) thus there is the combination of disorders of both lobes and of hyper- and hypoplastic conditions in the same individual; (2) the absence of any symptoms peculiar to pituitary derangement in unquestionable involvement of the gland; (3) the evidences of spontaneous arrest of the disease in many instances, and (4) the rather unusual occurrence of the full-fledged picture of functional disturbances.

It has been recognized from the first that mental disturbances —from listlessness and stupor to epilepsy and well-marked insanity—may be part of the symptom-complex of pituitary disorders, but comparatively little effort has been made until recently to search for pituitary symptoms in cases of mental disorder. No one etiological factor could be responsible for the various kinds of epilepsies and insanities, but it seems quite plausible that a derangement of the ductless glands may be responsible for some at least. Wenzel indeed, many years ago, looked on colloid collections in the pituitary as the cause of epilepsy. A study of

the autopsy findings at the Craig Colony for Epileptics, in New York, was made by Munson and Shaw,[1] who found occasional changes in the pituitary body, such for example as variation in weight. In the records of 1600 consecutive autopsies (1879–1912) at the Massachusetts State Hospital for Insane at Danvers, Bond[2] says there were 45 pituitary lesions, and out of 950 patients in the hospital in 1913, 10 exhibited symptoms of pituitary disorder. We cannot as yet draw any definite conclusions as to the relation between the hypophysis and mental derangements, but the circulatory disorders—the slow pulse, vasomotor stasis in the extremities, low blood-pressure and more or less adiposity—which accompany epilepsy, are at least suggestive of a certain relation. Only after a careful and systematic trial of the effects of glandular therapy and a more extensive study of autopsy findings, can we hope to determine the exact relation between pituitary disease, mental disorder, and epilepsy.

The roentgenology of sellar deformations has reached certain refinements, which are more of theoretical than practical value. In the first place, it is to be remembered that the normal sella turcica has a range varying from 8 to 13 mm. in its anteroposterior diameter, and from 6 to 10 mm. in depth. But as a matter of fact, in the vast majority of cases with suspicious pituitary symptoms, the expansion of the sella in one direction or another, is well beyond the extreme limits of the normal range. It is said to be characteristic of an intrasellar lesion, that the sella is deepened, its floor thinned and the dorsum sella elongated and attenuated. The anterior clinoid processes are usually deflected upward. In contrast to these structural alterations, the extrasellar lesion is attended with the widened orifice and the flattened floor, the tubercle sellæ is worn away and the anterior clinoid process is shortened and pointed. The distinction between intra- and extrasellar growth is not always possible, as we have been able to demonstrate in our own cases where a large extrasellar lesion may produce the sella deformation characteristic

[1] Arch. Int. Med., 1914, xiv, 393.
[2] Amer. Jour. Med. Sci., 1914, cxlvii, No. 4, p. 575.

of a true pituitary lesion. The fact that the order of sequence in the sellar changes may serve as a guide to the origin and seat of the tumor, is of little practical value, as the opportunity for observing the transition steps rarely is offered. The surgeon does not see cases in most instances until the disease is approaching the terminal stage. But in the matter of prognosis, I have found the roentgenogram of service by observing the effect of sellar enlargement upon the sphenoidal cells. If the sphenoidal cells have been encroached upon, flattened out and almost obliterated, one must not be too sanguine of the effects of sella decompression, as the available space for expansion and relief of pressure has been largely availed of. Hence little improvement will follow decompression. Sometimes we have found the roentgenogram of service during the course of an operation in orientating the sella floor. After penetrating the sphenoidal cells, a grooved director is introduced through the nose up to what is believed to be the middle of the floor of the sella. An *x*-ray exposure is made, and the accuracy or inaccuracy of direction is clearly depicted.

TREATMENT. With this brief review of the outward expression of lesions of the pituitary body, let us turn to the treatment. It is of course perfectly patent that no pharmaceutical preparation need be considered, but the question of glandular feeding may very properly be introduced at this point, preliminary to the discussion of the scope and possibilities of surgical therapy.

When the patient is not subject to intense headache or when vision is not threatened, and when there are no evidences of increasing intracranial tension, it has been my practice to advise recourse to glandular feeding in the vain hope, with one exception so far as my personal experience goes, of effectually ameliorating the condition. I say in the vain hope, for in none of the cases of pituitary disorders where the condition has advanced to the point of threatening vision or intense headache, have I seen the slightest benefit. The combination of thyroid with pituitary extract is advocated and the dosage, particularly of the thyroid, must be regulated according to the tolerance of the individual.

The selection of one lobe or another of the pituitary body instead of the entire gland is a difficult matter, since in most cases the clinical picture is a very complex one, and indicates involvement of both lobes. Theoretically, the anterior or posterior lobe may be given whenever the symptoms are at all definite, and indicate insufficiency of one or the other of the two lobes, or extract of the whole gland when there is evidence of deficient secretion of both parts. On the other hand, when the clinical signs point to a hyperactivity, as for example, in cases of acromegaly, which is now attributed to a hypersecretion of the pars anterior, feeding with the anterior lobe would be not only futile, but contra-indicated. Only in the instance of hypofunction, when, from primary hypoplasia or pressure the function of one or both lobes is more or less impaired, should we consider the propriety of prescribing glandular preparations. Included among the constitutional symptoms which may be benefited by glandular therapy to offset the influence of glandular insufficiency, are the polyurias, drowsiness, psychosis, sexual disturbances, amenorrhea and impotence, delayed or precocious puberty.

I advocate glandular feeding, however, with much hesitation and apprehension, for fear that it may become as serious in its effects as potassium iodid therapy in brain tumor. Certainly potassium iodid therapy, the screen behind which we conceal our inability to make a diagnosis or to localize the growth, has been responsible, more than any one factor, for the numberless pitiful cases of optic atrophy one sees when the brain tumor case first comes to the surgeon for relief. And I fear the same catastrophes if the profession generally, without an extensive experience in handling pituitary disease, without any knowledge of the danger signals, gains the impression that glandular feeding is a fitting treatment for pituitary affections.

But failing vision is only one of the possible disasters of delay and procrastination. Another, and one appreciated only by those who are dealing constantly with intracranial lesions, is increased intracranial pressure. The hazard of operations upon the cranial cavity is wrapped up in the physiology of intracranial

hypertension, and the greater the degree of intracranial tension, no matter what its source, the greater the risk of operative intervention.

Granted the ineffectiveness in some cases, and the impropriety in others, of glandular feeding, under what conditions should we have recourse to surgery? The mere acquisition of fat, believed to be an evidence of hypofunction of the posterior lobe, would of itself scarcely be considered an indication for surgical interference. Similarly, one might speak of sexual impotence, amenorrhea, or even acromegaly, which is often a self-limited disease. Theoretically, and analogous with the effects of partial thyroidectomy upon hyperthyroidism, the partial removal of a hyperplastic anterior lobe would exert a beneficial effect. We have under observation now one case in which this operation has been practised, and since the operation there has been no increase in the size of the hands or feet, which hitherto were palpably enlarged.

With perhaps one or two exceptions the supreme condition calling for relief by operation is visual disturbances with threatened loss of vision. How to deal with these should depend upon whether we are dealing with suprasellar tumors, or endosellar lesions. If the suprasellar tumor is unattended with enlargement of the sella turcica naturally a sella decompression would have little influence upon the condition. As a matter of fact, in the two cases in my series in which suprasellar tumors were actually disclosed at operation, there were marked sella deformities. At the present time our diagnostic facility has not developed to the point where we can distinguish between a suprasellar growth with secondary pituitary disturbances and primary intrasellar lesions. In my earliest surgical experience with pituitary disease I advocated the transfrontal approach to the sella turcica and devised a technic which made the sella safely accessible. Of the first eight operations by this technic, in three I found lesions the nature of which could only have been recognized by this route. One was a pituitary cyst, successfully evacuated, one a tumor of the middle fossa as large as a plum or peach, probably an endothelioma, and the third a large endothelioma, taking its

origin from the optic nerve. In three of the eight cases following partial removal of the sella contents there was either little relief or recurrence of symptoms, and resort was had later to transphenoidal hypophysotomy. This experience led me for the time being to abandon the transfrontal procedure until the time comes when we may be able to recognize clinically the presence of cysts that could only be evacuated by this route, and extrasellar tumors that have not reached the inoperable stage.

The surgery of pituitary lesions in my clinic has resolved itself largely into the invasion of the sella turcica by the transphenoidal endonasal route. This operation we have resorted to now routinely for the past two years, and have found it reasonably safe. In the majority of instances, I think I may say in every instance, save one, the principle motive for intervention was the hope of preserving what vision remained, for in many cases there was complete optic atrophy in one eye, and of restoring vision. By this method we have succeeded not only in improving vision, but in relieving headache and vomiting. Sometimes the improvement in vision is striking and is observed within a few hours of the operation. Sufficient time has not elapsed to observe the influence of the relief of pressure following sella decompression upon such distinctly glandular disturbances as have to do with the sexual sphere and with disturbances of metabolism. In appropriate cases after the operation glandular feeding is instituted.

Two procedures are to be considered, a sella decompression alone or with extirpation of the tumor. When the pituitary body is flattened out against the floor of the sella, a condition we have not yet recognized, the impropriety of proceeding further is self-evident. In other cases as much of the tumor as is available is extirpated. Our practice has been distinctly conservative, and I doubt whether in the absence of conditions threatening life, we should launch forth on too radical a course. The benignity of many pituitary lesions, and the comparative benignity of many malignant growths of the pituitary, may be offered as an argument in favor of conservative practise.

For the relief of subjective disturbances of intracranial tension temporal decompression naturally suggests itself, but the operation has been singularly ineffective. In one of my series headache was the most disturbing symptom—it was almost constant and often distressing, but a decompression failed to afford the slightest relief. This may be attributed to the fact that the tension of the dural capsule of the enlarged gland is uninfluenced by a subtemporal opening.

When there is an associated hydrocephalus, puncture of the corpus callosum will measurably relieve the symptoms of intracranial pressure. In two of my series, dilatation of the ventricles was a conspicuous feature, and in one of these, headache has been relieved, and optic atrophy arrested by callosal puncture. The condition was recognized before the operation by the atrophy of the inner table of the skull, and flattening of the convolutions, as revealed in the roentgenogram.

It must be remembered that we are still in the developmental stage of pituitary surgery, feeling our way along cautiously; the opinions we entertain today may not be those of tomorrow. I have felt hampered particularly by the lack of opportunity in any considerable number of cases, to study the morbid anatomy of pituitary disorders postmortem. There are all told but five available specimens in our laboratory of neuropathology, only two of these from our clinic. The advantages of studying the pathology in the living as compared with postmortem conditions, are recognized by surgeons generally, with reference to surgical lesions of the abdomen, but the very limited opportunity on the operating table in the transphenoidal route for getting a comprehensive picture of the size and relation of the pituitary enlargement to the pituitary body itself and to the surrounding structures is a distinct handicap in working out the many and intricate surgical problems in this particular field.

THE TRANSPHENOIDAL APPROACH TO THE PITUITARY[1]

By L. H. LANDON, M.D.

Mechanical measures must as yet be regarded as the most effective means at our disposal in the treatment, palliative and curative, of the vast majority of pituitary lesions. Whether or not as our knowledge of the functions and interdependence of the ductless glands, of the hypophysis in particular, and especially of the etiological factors involved in disease of this gland increases, rendering diagnosis a much earlier possibility, surgery will become of secondary importance to as yet unknown therapeutic agents is problematical but quite possible.

As it is, most cases come to our notice only after the appearance of those secondary or neighborhood symptoms dependent upon the mechanical disturbance of important structures outside the sella turcica but lying in close proximity to the gland. The mere abnormal accumulation of excessive subcutaneous fat, the sexual disturbances, the skeletal and other metabolic changes seen in preverted function, hyper- or hypo-, may be disturbing to the possessor but rarely cause him to seek surgical intervention. When however, those more serious and progressive symptoms occur as the result of an extension of the process beyond the confines of the sella, the serious nature of the malady is recognized.

The problems therefore in pituitary surgery have thus far resolved themselves mainly into the relief of these mechanical sequelæ, chiefly the preservation of vision, the relief of the general

[1] Read March 3, 1915.

and local intracranial pressure increase, and the rectification if possible of functional abnormalities.

The difficulties confronting the surgeon seeking adequate exposure of the hypophysis and its neighborhood are truly enormous. A superficial survey of the anatomy from the surgical viewpoint will make this more apparent and at the same time account for the numerous methods of approach, some good, some bad, which have been devised during the progress of the surgery of this gland.

By the ancients, the hypophysis was regarded as the seat of the soul and certain it is that if the relative value to the economy of various body structures is in some respects indicated by their protected positions, the pituitary must be regarded as of prime importance to the organism. It is situated in the most protected and inaccessable portion of the skull, almost in the centre of its base, within the bony sella turcica. A firm, fibrous dura surrounds it on all sides, a process of which, the diaphragma sellæ, stretching across above shuts it off entirely from the general cranial cavity except at one potential opening near the centre which permits the passage of the infundibular stalk attaching the hypophysis to the floor of the third ventricle. It is important to note that although surrounded by dura, the pia-arachnoid and hence the cerebrospinal space, is in relation only to the upper and slightly to the lateral aspects of the gland. Any intracranial approach must therefore pass through this space while it is possible to avoid it in the attack from below. Immediately in relation above the gland lies the optic chiasm or optic nerves as the case may be when the chiasm lies posteriorly, and the anterior cerebral arteries. Close at hand on either side are placed the cavernous sinuses and their venous tributaries, the third, fourth and sixth nerves, and the terminal portions of the internal carotid arteries. Any intracranial operation must therefore present the dangers of injury to any or all of these important structures.

Below the sellar floor are the sphenoid sinuses and more or less of the body of the sphenoid bone. An attack by way of the sinuses avoids many of the dangers of the intracranial route but with

the more likely possibility of a resulting meningitis especially if by chance the exploration extends to the opening of the subarachnoid space over the upper portion of the gland.

Of the intracranial routes, that proposed by Sir Victor Horsley was the first (1898), as he was also the first to publish results of the experimental removal of the gland (1886). Horsley's route was a lateral one by way of the subtemporal region through the middle fossa of the skull. Later Kiliahi (1904), Hartley (1904), and Krause (1906) all proposed an approach across the anterior cranial fossa. It is not our purpose to discuss the relative values or the results obtained with these various procedures. Suffice it to say that the intracranial method which has given the best results in the hands of competent operators has been that proposed by McArthur and later modified by Frazier.

A long step in the progress of hypophyseal surgery was, however, due to Schloffer (1906) who not only suggested the possible value of a partial extirpation of the gland to combat the progress of acromegaly, but carried out a transphenoidal approach by a method proposed some years before by Giordano (1897), which forms the basis of all other extracranial routes in that they all in common approach the sella through the sphenoid sinuses. This method of Schloffer was an extremely radical procedure including the turning down of the nose to the right, with exenteration of the entire left nasal cavity, septum, turbinates, the inner wall of the orbit and of the maxillary sinus, and the ethmoidal cells. This constituted the upper or superior nasal approach. Schloffer's method later underwent many modifications, notably those of Kocker, von Eiselsberg and Hochenegg. All these procedures were more or less permanently mutilating, dangerous in thier performance, unnecessary in their magnitude, and frequently followed by meningitis.

To Kanavel (1909) belongs the credit of first demonstrating the possibility of an approach by way of the inferior nares. This method contemplated the turning of the external nose upward in gaining access to the nasal cavities. The following year, Hirsch perfected and greatly simplified Kanavel's method in that the

entire operation is done through one nostril. About the same time Halstead proposed and used a sublabial incision to reach the nasal chamber. One or the other of these two latter inferior nasal methods is now usually employed. It is a slightly simplified method of Hirsch which is the subject of this paper. This operation, I have had the opportunity, through the kindness of Dr. Frazier, of employing in some twelve cases which occurred on his service at the University Hospital.

Preparation of Patient.—As in this operation our field lies entirely within the nose and its accessory sinuses, the sphenoid cavities, no less important than the operation itself is the careful local examination and minute care in preparation. It has been stated by careful observers that the normal healthy nasal cavities are sterile, but the probabilities of our having to deal with a normal and healthy nose are so few that we can in no case rely upon this supposition. Careful examination is made to exclude any evidences of an inflammatory condition, no matter how mild, of the mucous lining of the nose or any of its accessory cavities. If these are present, the operation should never be attempted until they have been completely eradicated. Again the examination should take note of any complicating endonasal deformities. Unusually large turbinates may require a preliminary resection some days prior to the operation itself. We have never found turbinectomy necessary to secure sufficient room and in this we have differed from Hirsch who seems to perform it routinely. A badly traumatically deflected septum may prolong the preliminary step unduly so that the operation cannot be completed at one sitting. The relations borne by the sinuses, ethmoid as well as sphenoid, to the sella turcica must be accurately determined and fixed in the mind of the operator. This is of course possible only by the aid of proper roentgenographic studies. The sella may bear varying relations to the sinus; it may be entirely behind, above, or in front of the sinus. The sinus may lie in close relation to the floor of the sella with only a thin plate intervening or a thick body of bone up to one-half inch may have to be traversed before the pituitary is reached. The knowledge of these relations

in each individual case is most important if we are to properly orientate ourselves during the operation. In one of our cases, an early experience, the sphenoid sinus was supposed to have been entered. As it was customary in our earlier operations to divide the procedure into two stages at the point when the sphenoid was entered, a grooved director was placed within the sinus and the patient roentgenographed. The tip of the probe lay within the middle ethmoid cells, far from the point desired. Had this line of attack been prolonged, irreparable damage would have resulted.

After all contra-indicating conditions have been eliminated, as long as possible prior to the operation, the nasal cavities are douched with 1 to 8000 potassium permanganate solution every three hours, each douching being followed by the careful inhalation of medicated oil from a nebulizer. Douching is preferred to the usual spray for fear that in careless hands undue force may wound the mucous membrane.

Position and Anesthetic.—The operation is performed in the sitting posture. Local anesthesia preceded one-half hour by the hypodermic administration of morphine sulphate, grain $\frac{1}{6}$, plus atropin sulphate, grain $\frac{1}{150}$, is used. After the exposed portions of the face and the vestibules of the nares have been painted with 5 per cent. tincture of iodin, cotton pledgets moistened with a 10 per cent. solution of cocain in 1 to 1000 adrenalin chloride are placed against the mucous membranes of the septum on both sides in their entirety. These are left in place for fifteen minutes when anesthesia is complete. As an additional precaution, at the end of this time from 1 to 2 c.c. of 0.5 per cent. novococaine solution are injected hypomucously on either side. This injection not only aids in the anesthesia but if properly placed will raise the mucoperichondrium from the underlying cartilage and bone, making their subsequent separation much easier. If properly carried out this anesthesia will last for from one and one-half to two hours. The protective hood is now lowered over the head and face of the patient leaving only the tip of the nose and nares exposed.

Operation. Through a single perpendicular incision in the septal mucoperichondrium, a half-inch within the left nostril, a submucous resection is done by the Ballenger method. Extreme care should be taken to avoid perforation of the mucoperichondrium and hence communication with the general nasal cavities except at the primary incision. Our guide to the sphenoid sinuses is the rostrum of the vomer which usully lies in close relation to their anterior wall. When this is reached in the removal of the bony septum, the mucoperichondrium is separated from their anterior walls on either side until the ostea are seen. The sinuses are now opened either by enlarging the ostea with punches, or by deliberately cleaving away the vomer with a chisel. This latter method has always been used by me and has always given a good opening into the sinus. Up to this point illumination is secured by reflected light from a head mirror. A modified Killian speculum carrying an incandescent light at its tip is now introduced between the mucous membranes. This two-bladed speculum is made especially heavy and rigid and by means of it the turbinates are flattened out on either side to the full capacity of the nasal cavities, exposing the sinus to the full extent of its anterior walls. Through this speculum and under direct vision, the remainder of the operation is completed. A sphenoid septum if present is broken down and the prominence of the bulging sellar floor is identified. The floor of the sella is opened with a chisel and the opening enlarged with special punches as far as possible in all directions. In many cases this is a very easy matter, as pressure atrophy of the bony floor has taken place leaving it of only egg-shell thickeness which is easily picked away. In some none of the floor remains and the tumor may occupy the sinus itself. If the sellar contents are under pressure, they prolapse to a greater or lesser extent into the sinus through the decompressive opening. The dural capsule is now slit with a crucial incision and its contents exposed. Unless unwarranted traumatism is done or too wide exploration attempted, the subarachnoid space is not opened. If this should occur, it is evidenced by the escape of cerebrospinal fluid and although this has occurred upon one or two occasions, it has, so

far as I know, never resulted in a persistent fistula. Hemorrhage is never of moment and oozing is easily controlled with adrenalin. At the conclusion of the operation, the field is dried, and the speculum removed when the mucous walls fall together. One or two stitches are placed in the primary incision to prevent retraction and to seal the wound. Drainage has never been necessary. It should be avoided as it increases the danger of infection. For twenty-four hours the nasal cavities are packed with bismuth-albolene gauze to hold the mucoperichondrial layers together and prevent oozing. General and local reaction following the operation are surprisingly slight and although the patients are kept in restraint for at least two weeks, they have no suffering. Slight swelling of the nose and headache for the first twenty-four hours are prevented or relieved by ice compresses.

In a few cases the addition of ether anesthesia will be found advisable during the actual exposure of the tumor. It is scarcely ever necessary to carry it beyond the phychic stage. As to whether or not the operation is done in one or two stages depends upon the difficulties met during the first part, the surity that one has entered the sphenoid sinus, the certainty of recognizing the sellar floor and the general condition of the patient.

What is the scope of the operation and what may be accomplished after exposure of the gland or tumor? This is perhaps the most important part of the procedure insofar as the judgment of the operator is concerned. First we must admit that no operative exposure of the pituitary has as yet been accomplished which will permit of a liberal exposure of the region of the sella or of any determination relatively of the size of a tumor or of the gland itself. The essential material advantage of this operation is the local decompression, producing an area of least resistence toward which enlargement of a tumor or of the gland may take place. This transfers the direction of encroachment and relieves the pressure upon the chiasm or nerves and other important neighborhood structures. It relieves tension upon the dural envelope, to which tension much of the severe headache in certain cases is ascribed. Fragmentary portions of a tumor, malignant or hypertrophic,

are removed with a sharp curet, and a cyst or cysts if present may be discovered and evacuated. As far as radical removal is concerned, only a small intrasellar growth or a cyst will permit of success. The degree of amelioration in malignant cases will of course depend upon the degree of decompression and the duration upon the rapidity of growth.

What other favorable results may be expected? Hirsch has carried out his operation fifty times in 37 cases with the following results: In 4 cases the operation had no effect. In 5 cases there were transient results for from four to six months. In 21 cases there was considerable and durable amelioration of symptoms, headache, drowsiness, mental torpor and weight. Some who were blind could see again, and two women with cessation of menstruation regained their periods after the operation.

In our own cases the results have been gratifying but not enough time has elapsed to determine their permanency. In all but one case, the headaches have been relieved. This is a case of acromegaly without ocular symptoms. It was the first case attempted and I am inclined to think that the opening into the sella was insufficient or that the capsule of the gland was not properly incised. In all with visual symptoms the progress has apparently been arrested, while in at least 2 cases the extent of recovery of vision has been truly remarkable.

The transphenoidal operation is undoubtedly the simplest procedure for the relief of sellar tumors and while the mortality seems high, by comparison it is much lower than that following any of the other operative routes, as evidenced by the following statistics collected by Hirsch:

Method.	No. cases.	Fatality.	Mortality, per cent.
Horsley	14	5	41.0
Krause	5	..	40.0
Schlaffer	49	17	34.7
Kanavel-Halstead	11	4	36.0
Cushing	29	4	13.8
Hirsch	37 (50 operations)	5	13.6—10

Unfortunately due to errors of judgment, enthusiasm, or too great confidence in the operation, in the death of 2 of our cases,

the mortality has been unfortunately increased above these latter figures of Hirsch. The total number of deaths in the twelve operations have been three. The first made an uneventful and perfect recovery up to the time of his discharge from the hospital at the end of two weeks. The first night out resulted in an acute rhinitis followed by a streptococcic meningitis from which he succumbed in forty-eight hours.

Of the other 2 cases mentioned, the first was delirious at the time of operating, extremely weak with frequent general convulsions and all the signs of the terminal stages of an extensive intracranial growth. In addition as a last resort, 75 mg. of radium were introduced into the tumor at the operation and left *in situ* for eighteen hours. He died on the second day. The third fatality was comparable to the second, the autopsy exposing a huge growth extending into the brain above, while the base of the skull including the sella, body of the sphenoid and basilar process were entirely destroyed by erosion. If we disregard these 2 most unfavorable and hopeless cases which I do not think we would now attempt, the mortality has been 8.3 per cent.

Since the reading of this paper I have operated upon an additional case with favorable results so far. This brings the mortality into the neighborhood of 7.6 per cent.

DISCUSSION

Dr. Alfred Stengel: These papers have been so excellent and so comprehensive, that as the hour is late I shall not greatly prolong the meeting, but I would enlarge just a little on the remark made by Dr. Frazier that there are more cases of pituitary disease or hypophysis disease than we have been inclined to suspect. The case under my care, which he described, is an illustration of a type that I think is far more common than we have heretofore believed. We have heard a good deal tonight about headaches, hemianopsia, blindness, etc., as symptoms of pituitary disease. The recognition of these unmistakable evidences of hypophyseal disease have opened the way to the discovery of pituitary or hypophysis disease in other forms. As the internist sees hypophysis disease it includes some other things, such as certain types of diabetes

or glucosuria, diabetes insipidus, cases of rather pronounced fatness, or patients who present certain other forms of structural abnormality. We are just beginning to know these cases, but I believe they are much more common than we suppose. I was struck in the case of my patient, whose photograph Dr. Frazier showed, by the resemblance it presented to a case of Cushing's. The case was a typical, though not advanced one of pituitary disease (fatness and sexual undevelopment) in a boy of nine years. While looking at the child in the presence of his father and mother my eye fell on the mother who was never supposed to have been ill and was not suspected of having this trouble, and I could not help seeing the resemblance between the mother and the child. The woman was much like the boy in features and very strikingly large, and the boy of nine bade fair to follow in that direction, though in a much more pronounced way. Cushing showed me a picture of this type of marked grade and then showed the pictures of the mother in which the condition was evident in a minor grade. No doubt the cases reported will open up in the future a wide recognition of lesser grades of pituitary disease and we shall learn more of the chemical disturbances incident to the disease. Up to the present we have learned only the symptomatology of tumors or cysts of the hypophysis, but these are doubtless perversions of function that are independent of tumor growth. There are diseases of the hypophysis that are not adenomatous. I am particularly struck with the fact that so few physicians have realized the existence of the type of pituitary or hypophysis disease in which diabetes insipidus is the clinical manifestation. So far as treatment is concerned we have to deal with that type which can be recognized, which is the tumor growth type, and we know nothing, comparatively speaking, about any other form. My own experience has been confined to only a few cases which have been strikingly lacking in results, except in one case which Dr. Frazier has shown and in which Dr. Thorington reports marked improvement in vision. As Dr. de Schweinitz has said, the visual fields change rapidly and this may have been merely an accident incident to observation on two successive occasions.

Dr. Charles K. Mills: As is well known, I do not perform any operations myself, and as is also well known probably, there is scarcely any sort of neurological operation which I have not had some of my friends among the surgeons do for me. In pituitary disease, on the whole, I have been fortunate in the work which has been done for me by surgeons, although the results have been by no means uniformly successful, so far as relief or cure is concerned. However, we could hardly expect this in the large majority of cases. When I have a well-defined case of dyspituitarism (for as Dr. Frazier says, they are mostly of this description,

that is, cases in which there is more or less commingling of hyper- and hypopituitarism) if with these manifestations symptoms described here this evening are present, I refer these cases after a short medical treatment to the surgeon, generally for decompressive surgical treatment. Especially do I follow this course when severe headache and certain forms of impairment of vision are present with the pituitary syndromes.

From looking on as neurologist at the operations done in cases in which I have been interested I have been favorably impressed with the fronto-orbital operation which Dr. Frazier uses.

Unless the reference to them by the speakers escaped me, I have heard tonight no mention of the uncinate symptoms so often observed in pituitary cases. As some here may remember I presented three or four years ago to the American Neurological Association a paper on the subject of the combination of uncinate and pituitary symptoms, or the pituitary-uncinate complex. I have had one or two cases with Dr. Frazier. One case I remember came into the hands of Dr. Cushing and was operated upon by him twice at least. I have two or three of these cases under observation now, in which are present the uncinate symptom-complex of Hughlings Jackson—the gustatory or olfactory symptoms or both in combination—with pituitary symptoms, the taste or smell phenomena being accompanied by the dreamy state and preceding in some instances attacks of Jacksonian spasm.

In this distinct type the question arises whether there is a primary sellar pituitary lesion with extrasellar invasion of other parts, or whether you have the sella turcica invaded by a tumor growing from the uncinate convolutions or that neighborhood. This is sometimes an important question for the neurologist to decide, as the decision has some influence upon the method of operation to be taken. As I believe, and as I have suggested to Dr. Frazier in one or two of these cases, in some instances it is better to do a double operation, an operation very low for the exposure of the frontotemporal region in addition to the direct pituitary operation, whatever this may be.

We have made much headway in recent years in our understanding of the subjects, both of pituitary function and disease through the combined results of clinical and surgical observations.

Dr. F. X. Dercum: I should like to ask Dr. Allen whether the extracranial, *i. e.*, the pharyngeal portion of the pituitary body, as it is called, was studied by him, and if so, what value he assigns to this structure. It would be quite important to know whether it undergoes changes when the intracranial pituitary is extirpated in dogs or other animals.

I think we should be very careful in making deductions from the symptoms which follow extirpations of ductless glands. For instance,

not the pituitary alone but a number of glands are concerned in the process of adiposis. In autopsies in adiposis dolorosa the pituitary gland is found enlarged in a small proportion of cases while changes are also found in the thyroid and adrenals; these are usually more marked than those in the pituitary. I know of no structure in which pathological changes are so difficult to determine as those in the pituitary. If the gland be grossly diseased and enlarged this is of course easily recognized, but in cases of dyspituitarism, in which the gland is unquestionably diseased but in which no enlargement is found, the interpretation of the findings is extremely difficult.

Dr. Mills's remarks remind me of a case of acromegaly in which the patient presented among other symptoms an epilepsy generalized in character. This epilepsy was always preceded by an odor which the patient was incapable of describing save as disgusting and horrible. This aura of smell lasted for a minute or more before unconsciousness supervened. In this instance the skiagraph revealed a greatly enlarged sella turcica and an operation for extirpation of the pituitary was clearly indicated, but the patient's consent to operation could not be secured. Thyroid treatment, as carried out in the case of Dr. de Schweinitz, was instituted but without result.

Dr. William S. Wadsworth: It seems to me desirable that something should be said about that large part of the whole problem of the pituitary body which has not been touched on this evening.

It is astonishing how little of the anatomy of this body is discussed. The relations which it holds to the circulation of the brain is not adequately pictured or described in any work on anatomy that I know of.

The evident association of the organ with the blood-pressure has recently been positively demonstrated pharmacologically, yet the physiologists do not recognize the type of apparatus in which it is an integral part. The pathologists pay but scant attention to the conditions that are less marked than actual tumor.

I have been in the habit of demonstrating the relations of this body to the arteries which supply the brain for the past twelve years and I am compelled to wonder how its significance as a part of the circulatory apparatus of the brain could have been so long overlooked.

The way this little mass of combined nervous and glandular tissue is placed between the loops of the carotid arteries and the way the loops and body are placed in a remarkably constructed capsule of sculptural bone and properly distributed membranous walls and fenestrated roof should at least suggest to thinking persons that such an elaborate mechanism cannot possibly be entirely purposeless. It is interesting to note that other allied branches of the medical group have already

noted the relation of this organ to the circulation. It has been long known that epilepsy in horses has been found to be associated with pituitary disease. I have a number of times been able to clearly associate mental states with changes in this body from the history to determine that a lesion would be found—and it was found—and from a lesion found at the postmortem to determine that certain mental symptoms should have been noted, and subsequently obtained history confirmed this, even to the correspondence of duration of the conditions and lesion. We hope that this enthusiasm about a part of the natural history of the pituitary will finally lead to the full realization of its complete physiology.

Dr. Allen (closing): In answer to Dr. Dercum I would say that the extrapharyngeal portion of the pituitary body is not well developed. I do not believe that it would be often found as believed by many. I do not believe there is in literature a record of a parahypophysis.

SARCOMATOUS DEGENERATION OF A FIBROMA OF THE UTERUS FIVE YEARS AFTER *X*-RAY TREATMENT FOR PRESSURE AND HEMORRHAGE[1]

By GEORGE ERETY SHOEMAKER, M.D.

The subject of the treatment of fibromata of the uterus by non-surgical methods is one of such importance that all data having a bearing upon the subsequent behavior of such growths should be carefully recorded. The time must of necessity be very great which must elapse in any individual case before the final evidence can be secured as to the subsequent degenerations, for example, after the application of *x*-rays or radium. Of peculiar importance is the question whether the sarcomatous or other forms of malignant degeneration are less liable to occur after such treatment, or whether they occur at all.

While no exact percentage can be given, it is certain that sarcomatous degeneration is a definite risk in untreated fibroma of the uterus.

Many series of reports, especially those of aggregates made up from many sources, are almost without statistical value, as for a long time in many clinics, routine examination of all tumors was not made, only those being studied which looked suspicious to the eye.

Winter,[2] in a series of 253 cases examined systematically, found 4.3 per cent. of sarcoma.

Ellice MacDonald[3] analyzed 700 carefully studied cases and

[1] Read April 7, 1915.
[2] Zeitschr. f. Geburtsh. u. Gynäk., 1906, lvii, 2, p. 23.
[3] Transactions, Section on Obstetrics and Diseases of Women, 1909, p. 93-112.

found malignancy complicating in 5 per cent. of all cases, though but 1 per cent. were sarcomatous. Necrotic changes were found in 8 per cent.

Certain writers have argued that after *x*-ray treatment no cases of malignancy have been observed. It is obvious, however, that not until the end of a patient's life can it be stated that malignant degeneration will not occur. The *x*-ray treatment of fibromata has been carried out for comparatively but few years, so that it will be many years yet before the final outcome of these treated cases can be known. The difficulty is further increased by the fact that those patients who have subsequent trouble after any form of treatment, operative or otherwise, usually consult other physicians. We get other men's postoperative hernias, rarely our own. It will not do, however, to infer that we never have any.

I desire to put on record as a contribution to the subject, the history of a patient known through conference with her physicians for many years, and who finally developed sarcoma in a fibroid tumor about seven years after *x*-ray treatment was begun and five years after it was stopped.

The patient, Mrs. I. H., now aged fifty-six years, married, one child, one miscarriage, underwent at my hands, nineteen years ago, an operation for laceration of the perineum, in consultation with Dr. John H. Musser. She then had no tumor. She was not seen again until April, 1914, when she was referred by other physicians for operation, and I removed a large tumor which proved to be a sarcomatous degeneration of a multiple fibroid of the uterus. The following interesting history was obtained of her experiences and treatment at the hands of various physicians during the intervening years. There had been one attack of gall-bladder inflammation and jaundice in October, 1913.

The menstrual flow had remained normal until early in 1907, when it increased and also partial suppression of urine occurred. Examination by Dr. Rachel Williams discovered a large fibroma of the uterus, tightly filling the lower abdomen, and pressing upon the urinary tract. She was then subjected to electrical treatment for the tumor by an electric specialist who writes on cataphoresis. This treatment is said to have continued for nearly a year, one or two treatments a week, with no effect observed.

In November, 1907, *x*-ray treatments were undertaken by Dr. Newcomet to diminish the size of the growth; the patient being referred to him by Dr. Williams. He writes that she received fifty-four treatments at this period; ten minutes each; twenty inches distance; spark gap four inches. In spite of leather protection for the skin, considerable reaction was produced, followed by bronzing and local dilatation of vessels; which effects are, by the way, still observable. He further states that the tumor was reduced to about one-fourth its size, and hemorrhage was controlled by the first of April, 1908. Nine months later, in January, 1909, the tumor grew again to the level of the umbilicus and eleven more treatments were given by Dr. Newcomet. In November, 1909, he found the growth just above the pelvic brim. It then apparently remained quiescent until November, 1912, when it began to grow; hemorrhage reappeared in December, 1913. Dr. Newcomet refused to administer *x*-rays longer, and advised operation. The patient delayed, seeking other opinion, but, as has been stated, finally reached me for operation in April, 1914.

On examination the bleeding was now found very dark brownish or black in color; there was no odor; no leucorrhea; the systolic blood-pressure was 180; the patient was quite stout; the heart sounds good. The abdomen showed a number of hemorrhagic spots in the skin apparently produced by the *x*-rays, and a number of reddish spots were scattered over the mucous membrane of the cervix and upper vagina. The tumor was round, smooth, moderately fixed, a little irregular in outline, hard, reaching to the umbilicus, no infiltration of surrounding tissue. Advice was immediate removal of a growing tumor which, at the age of fifty-six years, had shown signs of activity and had resumed bleeding after a cessation of five years.

A very smooth recovery followed abdominal hysterectomy. There were no parietal adhesions. Dr. William Evans and Dr. Rachel Williams were present. Two days ago, one year after operation, she reported herself entirely well.

Dr. Damon B. Pfeiffer, the pathologist of the Presbyterian hospital, has kindly furnished the following report:

The specimen consists of a large, irregularly shaped uterus, measuring roughly 15 x 10 cm. The greater part of the mass consists of a rounded tumor, which on section presents the appearance of a myoma. There is no sharp demarcation between the mass and the uterine wall. Several small subperitoneal nodules are also present. The uterine cavity is opened. The endometrium presents no abnormalities. The Fallopian tube is distorted and somewhat thickened. The ovary appears normal.

Microscopically, the ovary is normal, the tube is moderately thickened and fibrous, presumably the result of chronic interstitial salpingitis sometime in the past. Sections from the large tumor or mass show, in some places, areas of hyaline degeneration and in other portions the growth is extremely cellular. The cells are relatively large, but vary considerably in size, appearance, and nuclear content. Many mitotic figures can be seen, and at the margin of such actively proliferating areas, there can be seen at times evidences of invasion of the older and less cellular portions of the growth. There is no sign of extracapsular invasion or metastasis, but the evidences of rapid atypical proliferation above mentioned warrant the belief that sarcomatous transformation has occurred.

Conclusion. It is the complications of fibroid tumors which render them important. Hemorrhage, pressure; intestinal adhesions, stasis, or obstruction; pressure on the uterus or bladder; secondary renal disease; heart lesions; salpingitis; appendicitis; pregnancy; necrosis or other forms of degeneration; associated malignancy may be mentioned.

In the study of end results time is necessary. That treatment must be advised which best eliminates most complications as well as the tumor, and which preserves, if possible, sexual characteristics by its technique. This treatment in a large proportion of cases is surgical.

DISCUSSION

Dr. John A. McGlinn: The question which Dr. Shoemaker raises in reference to sarcomatous degeneration and fibroid tumors of the uterus after *x*-ray treatment is an important one. We must acknowledge that fibroid tumors of the uterus can be cured by *x*-ray therapy and that the method has a very important place in the treatment of neoplasms. Whether this treatment, however, can entirely replace surgery is still problematical. Hysterectomy for fibroids has a definite mortality. Treatment by the *x*-ray has practically no immediate mortality. At first sight this statement might seem to settle the whole question in favor of the *x*-ray treatment. Statistics by men favoring the use of the *x*-ray place the death rate of hysterectomy at 5 per cent. These figures are based on the operative results of the gynecic surgeon,

the general surgeon, and the occasional operator. I am satisfied that the death-rate among trained gynecic surgeons is not over 1.5 to 2 per cent. Assuming, however, the 5 per cent. mortality, it is claimed by the *x*-ray therapeutists that the only thing to fear from their treatment is the presence of sarcoma at the time of the treatment. They state that sarcoma occurs in but 2 per cent. of all cases, and that if every case of sarcoma dies, there will still be an advantage of 3 per cent. over surgery. This reasoning is entirely fallacious. Sarcoma is not the only cause of death when surgery is used; the death-rate is augmented by other degenerative changes in the tumor and by intra-abdominal complications. The majority of *x*-ray therapeutists advise against the use of the *x*-rays in the presence of the majority of degenerative changes, so that surgery has to be used in the very case where the *x*-rays are not applicable and at the same time bear the onus of a comparatively high death-rate. Again, according to the statistics of Mayer, *x*-rays cause the entire disappearance of a tumor in comparatively few cases, whereas surgery, if it does not kill, cures absolutely all cases in which it is used. I am well aware that statistics can be quoted showing that the cases which have been treated by the *x*-rays have not shown late degenerative changes. However, Dr. Shoemaker reports such a case tonight and there are other cases known both published and unpublished. At the present time I believe that surgery is the best treatment for fibroid tumors of the uterus unless the patient is in such a condition as to absolutely contra-indicate its use.

Dr. Shoemaker (closing): During one month this winter I successfully did hysterectomy for four fibroids complicated with large cysts or large pelvic abscesses. This illustrates that the complications are often very formidable and that they are very common.

THE ORGANIZATION AND ACTIVITIES OF THE INTERNATIONAL HEALTH COMMISSION[1]

By JOHN A. FERRELL, M.D.
ASSISTANT DIRECTOR-GENERAL, INTERNATIONAL HEALTH COMMISSION

At the suggestion of the chairman of your Committee on Public Health, I shall attempt to outline the development of the International Health Commission.

This commission was created in June, 1913, by the Rockefeller Foundation as its first important act after receiving a charter from the State of New York. Its expressed object is "The promoting of public sanitation and the spread of the knowledge of scientific medicine." Its immediate task contemplates the extension of measures for the relief and control of uncinariasis, or hookworm disease, to those countries and peoples where conditions invite. This phase of the work is already well under way. Active measures are in progress in several territorial units in the Southern States, Central America, the West Indies, British Guiana, in South America, and Egypt; and other countries have signified a desire to have the coöperation of the International Health Commission.

In order to give a clear understanding of the plan of organization and the working methods of this Commission, I shall review briefly the work of the Rockefeller Sanitary Commission, from which it has developed as a natural outgrowth. The Sanitary Commission was organized by Mr. John D. Rockefeller in 1909, and granted $1,000,000 to be used during the ensuing five years toward the eradication of hookworm disease in the United States.

[1] Read April 7, 1915.

This commission, it will be recalled, was composed of thirteen of the country's leading educators, physicians, and business men.

Mr. Wickliffe Rose, Executive Secretary of the Southern Education Board and General Agent of the Peabody Education Fund, was selected as administrative head of the work, with the title of administrative secretary. Mr. Frederick T. Gates, adviser to Mr. Rockfeller and the chairman of the General Education Board, was elected chairman. As scientific secretary, Dr. Charles W. Stiles was elected. It was Dr. Stiles who discovered the presence and prevalence of the disease in the South; identified as its cause a new type of hookworm termed by him the Necator americanus, and did much to centre the attention of the profession, the public, and Mr. Rockefeller's advisers on its baneful influences.

Mr. Rose opened offices in Washington in January, 1910, and proceeded to organize the work. For obvious reasons, the State Board of Health of each State was selected as the agency through which to undertake the work. Where a health department was weak, he endeavored to aid in strengthening it; and where there was no health department, he sought to help lay the foundations for developing one. The work was always conducted in the name of the State Board of Health. In each of the eleven States with which the commission coöperated, a State director was appointed by the joint action of the public health authorities and the commission. This director became a State official—an officer of the State Department of Health—clothed with the powers and responsibilities of the office. He was the organizing and directing head of all the work in the State for the eradication of hookworm disease, and was responsible for results. He worked under the general supervision of the State Department; he made reports quarterly to the State Department, and through the department to the commission. Under his direct supervision was a force of from three to six physicians as field directors, each of whom was generally assisted by one or two trained microscopists.

On this general plan, eleven States invited and received the coöperation for the Commission: Virginia, North Carolina,

Georgia, South Carolina, Tennessee, Arkansas, Mississippi, Alabama, and Louisiana between February and November, 1910, and Kentucky and Texas in 1912. The remainder of 1910 and a portion of 1911 were devoted to perfecting the State organizations, to educational propaganda, to survey work, and to the trying out of working methods.

In beginning the work the coöperation of the physicians, the educational forces, and the press were successfully enlisted. The educated public soon began to regard hookworm disease as a problem worthy of serious consideration. Working methods were gradually developed on the basis of actual experience under varying conditions. These methods have been growing more systematic; the efforts more intensive; and the results more definite. The work in the beginning consisted very largely in visiting physicians, interviewing them, demonstrating the microscopic technique in recognizing the disease, and urging physicians to make examination for its presence a routine in their practice. The essential facts about the disease were prepared in popular form and distributed broadcast over the State—through the newspapers, in leaflets and pamphlets, and by means of circular letters. Lectures to public audiences and to schools were employed as a feature of the work at this stage. Soon the laity was ready to aid in determining the extent to which the disease prevailed; that is to say, specimens for examination could be obtained with reasonable effort. The State militia was first examined; then children in the various orphanages. When these investigations were completed, and the results published, it was found feasible to have the children in the public schools examined. Squeamishness began to disappear, and the work of examining school children proceeded rapidly. A group, usually of two hundred children or more, taken at random, was examined in every county, or at least in representative counties. Thus the prevalence and distribution of the disease were established with reasonable accuracy. In visiting the schools the field directors also inspected the sanitary conditions of the country homes on the roadside, and recorded their observations in each instance.

At this juncture, stock was taken. It was observed that the survey work was highly satisfactory. The disease, varying in different localities within the State and even within the counties, was found to exist among from 10 to 90 per cent. of the people. But the record of cures was small. In December, 1910, Mississippi tried, for indigent cases, the dispensary plan that had worked so successfully in Porto Rico for the whole of the infected population. It was found to be very satisfactory in that State, not only for the indigent cases but for all who applied. It was soon tried elsewhere, and speedily became in all the States the agency around which the chief activities centred. It provided a means for effective teaching by actual demonstration. It is still employed in some of the States, which are completing the work with aid from the International Health Commission, in a few of the heavily infected counties that could not be reached before December 31, 1914, which marked the close of the five-year period covered by the pledge of Mr. Rockefeller to the Rockefeller Sanitary Commission. A summary of the work through the dispensaries and through the increased activities of the physicians showed, by the close of 1914, that much had been accomplished in the South in treating the disease. The number of persons microscopically examined was 1,273,850. The number of persons treated and reported was 694,516. Of these, 254,118 were treated and voluntarily reported by the physicians, and 440,398 were treated in the dispensaries. This county dispensary work was very strenuous for the field forces. County appropriations for local expenses had to be secured; the campaigns had to be advertised and wide interest quickly created. A different dispensary had to be reached every day, often by traveling over miles of rough roads; frequently from one to five hundred people had to be examined during a day; lectured to; the infected ones treated; and a complete and accurate record of each case kept. This meant that the men were often out on the day's task from dawn until long after nightfall; but they loved the work and were convinced that the effort was well worth while. It is to be doubted if an equal number of men could have been found who would

have worked harder, or more effectively, or who would have accomplished so much in the same length of time by any other methods. The population and area to be reached were vast; the funds, and consequently the size of the working force, were limited; the time for completing the work was short; and the county dispensary campaigns were consequently limited to periods ranging from four to eight weeks—a time insufficient to develop satisfactorily the sanitary features of the campaign along with the curative measures.

Obviously, the next development in methods called for a lengthening of the working period; limiting the area to be worked; intensifying the efforts, and putting into effect both curative and sanitary measures. This modified plan of work was very satisfactorily developed, during the closing months of the Rockefeller Sanitary Commission, in four States, which were early in completing the dispensary work. It was completed, before the close of 1914, in twelve communities, each having an area averaging in size about thirty-two square miles and an average population exceeding a thousand persons (1025 to be exact). The working period in each averaged about four months. The work was done by a field director, who in some cases was aided by a microscopist. Of the 12,305 persons in the twelve communities, 75 per cent. were examined; 26 per cent. were found infected; and 94 per cent. of these were treated and probably cured; 29 per cent. of these were actually reëxamined after a course of treatment and all found to be cured.

In these communities there were 2257 homes; 50 per cent. of them in the beginning had no kind of a privy, and the privies found were seldom if ever sanitary. When the work closed, 88 per cent. of the homes had privies and 81 per cent. of these were of an improved type. The work in some communities was, of course, further advanced than in others. In fully a third of the communities every family had an improved privy, and every person found infected was treated.

This intensive work deserves special attention. It has been carried one step further by British Guiana. In selected areas

of British Guiana there are two staffs at work, under the general supervision of the Surgeon-General. The sanitary staff, financed by the government, enters the area first. It gives the area a thorough cleansing; attends to drainage, and enforces compulsory measures requiring every family to provide itself with an approved privy, and to use it and care for it. When this staff completes its work it moves into another area, leaving in the district a sufficient number of sanitary inspectors, employed permanently by the government, to insure the maintenance of the improved sanitary conditions.

The second staff is medical, and is financed by the International Health Commission. It aims at the examination of every person in the working area, and the treatment until cured of every person found infected.

This plan insures the development of adequate public health agencies by the government, which will carry on the work after the commission has transferred its aid to other fields and leaves to the local organization the enforcement of public health laws. The agency supported by the commission can be temporary, and it depends for its success on the voluntary coöperation of the people. Both staffs have made admirable successes, and there seems much promise that a wider application can be given to the plan.

Return for a moment to the Rockefeller Sanitary Commission. Its work *per se* accomplished gratifying results. Many observers, state, however, that the by-products have greatly exceeded in importance the tangible results with hookworm disease as published in the records of the State Boards of Health and in the reports of the Rockefeller Sanitary Commission. To give an illustration of this: it was found that the available funds for public health work in the eleven Southern States where aid was given amounted in 1910 to $216,195, and in 1914 to $392,364, an increase of 81 per cent. in less than five years. Of course, the commission does not assume the credit for this increase; it was wholly voluntary on the part of the States. It may be, however, that the States were stimulated by the spirit which pervaded the

forces devoted to measures for the control of hookworm disease. At any rate, the health departments are much stronger now than they were five years ago.

One incidental service of the Rockefeller Sanitary Commission to the public health agencies of the South and nation has been the bringing into the field of public health work of nearly one hundred carefully selected young physicians. The large majority of them have acquired a love for the work; an appreciation of the broad possibilities it offers for service to man; and more than a third of them have chosen it as a career, and have identified themselves with the State or national public health organizations.

The Rockefeller Sanitary Commission accomplished all that was expected by its founder and paved the way for the International Health Commission. Mr. Rose studied the work in all the States very closely, and correlated it by acquainting all the directors with any significant method employed by any one. His suggestions for increasing efficiency came to the State directors from time to time. They were not imperative. They usually carried by their own force. Occasionally, he called the workers together for conferences, when there would be round-table discussions, exchanges of experiences; and usually out of these conferences there developed more effective, more uniform, and more systematic working plans.

These fundamental policies which guided the Rockefeller Sanitary Commission are being adhered to in the development of the International Health Commission. They have worked satisfactorily thus far in dealing with a single problem in preventive medicine in the international field. They will probably apply with equal force to other public health problems with which the commission will deal in the course of its development.

Having described for you the ground-work on which the International Health Commission rests, and outlined the policies which are guiding its organization, I can tell the story of its activities to date in a few words.

In considering this larger work, Mr. Rose, in 1911, set to work to collect, from all countries of the world, the available infor-

mation on the distribution and prevalence of hookworm disease; the extent to which it was a handicap to the health and working efficiency of the people; the agencies at work toward its control; the results secured; and the methods employed. The results of this study were published in 1911. They indicated that the disease prevails in a belt of territory encircling the earth for 30 degrees on either side of the equator, inhabited by more than 1,000,000,000 people; that "the infection in some nations rises to nearly 90 per cent. of the entire population"; that the disease has probably been an important factor in retarding the economic, social, intellectual, and moral progress of mankind; and that "little or nothing is being done toward its arrest or prevention."

Owing to the time consumed in getting the Rockefeller Foundation chartered the International Health Commission was not organized until June 27, 1913. The members are:

John D. Rockefeller, Jr., chairman; Jerome D. Greene, recording secretary; Wickliffe Rose, director-general; Charles W. Eliot, Simon Flexner, Frederick T. Gates, William C. Gorgas, Charles O. Heydt, David F. Houston, Starr J. Murphy, Walter H. Page, William H. Welch.

In July, 1913, I went to Washington to give assistance in directing the work of the Rockefeller Sanitary Commission, and to become later the assistant director-general of the international Health Commission. This relieved Mr. Rose, so that he could make several journeys to foreign countries. He proceeded to London, in August, on invitation, with a view to establishing work in the English dependencies. The stability of the government and the official use of the English language made them a most suitable field for beginning work. A series of conferences had been arranged for him with groups of scientists, physicians, and government officials, the most important, with respect to action taken, being a dinner given by Ambassador Page—himself a member of the Commission—on August 13. Mr. Rose told, while there, of what had been done in the South; described the plan followed, and indicated that the International Health Commission was prepared to coöperate with the English government

on a similar basis. The proposition was accepted with eagerness; the government expressed its appreciation, pledged its active coöperation in the work, and appointed an advisory committee to coöperate with the commission in the colonies.

The British West Indies appeared to all the logical region for beginning work. Accordingly, Mr. Rose, in October, visited seven of the colonies: Barbadoes, Trinidad, British Guiana, Grenada, St. Vincent, St. Lucia, and Antigua. He desired to make a first-hand survey of conditions. He obtained a general view of the country and established an acquaintance with the officials and the working population. He observed the conditions of infection, and discussed working plans with the medical officers. In 1914 he spent about half the year on a journey around the world, visiting a number of countries, giving special consideration to Egypt, Ceylon, the Federated Malay States, and the Philippine Islands.

In the meantime the work of organization had been taking definite shape, and work was getting well under way in some of the colonies. Early in March, Dr. J. H. White was secured for a year from the United States Public Health Service to undertake the establishment of work in certain of the Latin-American countries. Here, as elsewhere, the commission did not enter the field without first being invited by the government, and receiving assurance of coöperation in the work undertaken. Dr. White had an intimate acquaintance with the Latin-American people, which enabled him to lay the ground-work successfully, and develop excellent working forces for Panama, Costa Rica, Nicaragua, and Guatemala before the close of his year's work with the commission. These republics will afford nuclei from which operations can spread to the other Latin-American republics as conditions warrant.

In the West Indies, Dr. H. H. Howard is now directing the work. He received his training in the commission's service in the South. On government invitation, he aided in organizing the work in British Guiana, which I have already mentioned. Active measures are now in operation or pending for six of the

West Indian colonies, and work will be under way within a few weeks in Dutch Guiana. In general, the working plan followed in British Guiana is contemplated in all this field.

The East presents an enormous field for work, which in many respects offers very difficult problems. For this post the Commission secured Dr. Victor G. Heiser, of the United States Public Health Service, who as Director of the Bureau of Public Health in the Philippines during the past twelve years, has dealt successfully with the more or less primitive native population and developed a highly efficient department of health. He is to give general supervision to the activities previously started in Egypt, and immediate direction to the extension of the work to other countries of the East as conditions favor.

It may be interesting to know that the work of the present year will cost the commission approximately $400,000, which amount is supplied by the Rockefeller Foundation. It is expected that the funds will be increased from year to year with the growth of the commission's work.

Doubtless one will be disposed to inquire what other fields of activities will be entered by the commission. Frankly, I do not know. Mr. Rose, the director-general, is open to suggestions. Measures that may now or ultimately be of international scope would be viewed with greatest interest. It has been told how aid is already given toward the development of public health agencies in several countries. This kind of work will, of course, be continued on one plan or another.

The director-general has been giving considerable thought to the development of facilities for adequately training workers for the many tasks in the field of preventive medicine. He recognizes also, as very pressing in many countries, the need of facilities for the care of the sick. This field would call for strengthening or establishing medical schools, hospitals, and clinics, and the training of natives to operate them. The attack on hookworm disease has led also to the consideration of a similar attack on other diseases, such, for example, as yellow fever or malaria. Entrance into any of these fields, I think, would not be expected

except on the basis of careful study and the maturing of definite plans. It might develop that other fields will present themselves which offer more fruitful effort in accord with the paramount aim of the commission, which is to help the countries to help themselves in bringing into activity their own working agencies, with their own resources.

RECENT PUBLIC HEALTH WORK IN THE UNITED STATES ESPECIALLY IN RELATION TO INFANT MORTALITY[1]

By JOSEPH S. NEFF, M.D., LL.D., D.P.H.

An address on the progress of Public Health Work, which I have been asked to present this evening, is perforce, historical—a compilation of facts which may not be of much interest to the expert, yet may be of some value to the lay physician. The knowledge of the vast amount of time, energy and work, and results accomplished may induce him to take some part in the Public Health Campaign, thereby aiding those working along similar lines in solving the serious problems that confront them.

The great deterrents to progress of public health work in this country have been political influence or control over public health officials; and ignorance of the people, and therefore the government, in the economic value of life and health. This becomes apparent in the study of public hygiene, and is shown conclusively by the comparison of results in various communities, both in this country and abroad, and especially in relation to the infant welfare movement.

The latter is shown most conclusively by the history of our own national government. Our statesmen, not appreciating Lord Beaconsfield's well-known saying "that public health is the foundation on which rests the happiness of the people and the power of the country; the care of the public health is the first duty of the statesman," have conserved our forests, our mineral resources, our lands, our streams, and our animals. "But man,

[1] Read April 7, 1915.

for whom all these should be conserved, is for the most part neglected, or left for the last consideration." Commercialism is still in the ascendant, as is shown by the millions annually appropriated by the national government for the protection of crops and animals, owing to their commercial value, compared with the paltry thousands appropriated for conservation of health and life of man, whose monetary value is not considered. Yet, it has been demonstrated by Professor Irving Fisher and others that in the United States approximately 3,000,000 people are constantly sick, at least one-third of whom are in the working period of life. Allowing for the non-employment of one-quarter of these, and assuming the average annual earnings to be $700, we find over $500,000,000 to be the minimum loss of wages, in addition to which the cost of medical attendance and nursing must be added; an annual loss to the nation of great magnitude. This same policy holds true in our municipalities. Appropriations for city improvements, protection of property, and development of ports in seaport cities, are large, for such development increases trade and adds to the commercial standing of the city, while far more important from an economic view is the prevention of sickness and mortality, especially of the wage-earner. Yet, as the commercial value of health and life is not fully realized, appropriations to municipal health departments are exceedingly small.

Notwithstanding this attitude, great progress has been made in sanitary science, more particularly in European countries, where health work has come, largely, under national control and is free from local political conditions. It is a rare thing today to find in most Continental cities a health officer who has not had special collegiate training for his work. The colleges in this country are not to blame, as many have already instituted courses, and confer degrees of "Doctor of Public Health" and "Doctor of Public Hygiene;" but our young men will not give years for their proper education for positions of this character, the tenure of which depends not upon efficiency, but upon political influence. This is the condition in the majority of our cities, although, happily, there are numerous exceptions.

The remedy for this evil lies in the organization of a national bureau or department of health, under whose general control all appointments should be made through civil service, to be terminated only by malfeasance in office, inefficiency, resignation, or death. Coöperation and aid of the national authorities would soon educate the community to abandon any local legislation that would not be in conformance with such organization. "In diseases which can travel from state to state, in diseases which can jeopardize the welfare of a commonwealth as a whole, state lines should not be considered." Municipal, county and state boards of health are phases in the development of a perfected whole, and should always exist, but hold the same relation to a national department of health that our cities, counties, and states do to our national government.

The many separate government bureaus now engaged in independent health work should be consolidated and coördinated in this national department of health, and have at least the authority over public health that the Inter-State Commerce Commission has over commerce. "Control of inter-state stream pollution would markedly decrease typhoid fever, control of quarantine and inter-state common carriers would remove a menace to the health of the travelling public. The coalition of investigation and coöperation with the many unrelated biological and pathological, federal, state, and private laboratories, would prove of inestimable value." These are but a few illustrations advanced as an argument for the creation of such a national department.

The twelfth census (1900) showed in some cities an annual death-rate in children under five years of age of over 100 per thousand of population. The fact that many of these deaths were preventable attracted attention, especially as the largest proportion of this mortality was in ages under one year, 25 per cent. of which were from diarrhea and enteritis, largely preventable. This great and needless mortality, constituting over 30 per cent. of the total deaths of the United States, attracted public attention, and it was therefore in the early part of the present century that the first concentrated efforts were made to conserve child life.

The following tables are presented as a means of comparing results in our larger cities.

TABLE 1—DEATHS UNDER ONE YEAR OF AGE

Cities.	Average number of deaths of infants under 1 year of age per 100 deaths from all causes.			Per cent. change.	
	1901 to 1905.	1906 to 1910.	1911 to 1913.	1906 to 1910 from 1901 to 1905	1911 to 1913 from 1906 to 1910.
Atlanta	19.38	17.56	15.40	− 9.39	−12.30
Baltimore	22.58	21.38	19.06	− 5.32	−10.85
Boston	20.20	20.68	18.57	+ 2.38	−10.20
Buffalo	22.68	24.06	22.00	+ 6.08	− 8.56
Chicago	20.10	21.12	19.50	+ 5.07	− 7.67
Cincinnati	14.94	14.66	12.00	− 1.87	−18.14
Cleveland	25.02	25.14	22.00	+ 0.48	−12.49
Denver	13.38	13.34	12.20	− 0.30	− 8.55
Detroit	25.76	27.98	25.90	+ 8.62	− 7.43
Indianapolis	17.38	14.66	12.37	−15.65	−15.62
Jersey City	22.22	22.01	20.14	− 0.95	− 8.49
Kansas City, Mo.	16.42	16.40	15.40	− 0.12	− 6.10
Los Angeles	9.60	11.50	10.77	+19.79	− 6.35
Louisville	16.50	14.10	12.27	−14.55	−12.98
Milwaukee	26.08	26.62	25.50	+ 2.07	− 4.21
Minneapolis	14.86	15.72	15.90	+ 5.79	+ 1.15
New Haven	20.02	18.66	17.23	− 6.79	− 7.66
New Orleans	16.22	15.78	13.13	− 2.71	−16.79
New York	21.78	21.78	19.33	0.0	−11.24
Newark	20.60	21.10	19.73	+ 2.43	− 6.49
Philadelphia	18.98	20.44	17.73	+ 7.69	−13.25
Pittsburgh	24.14	24.26	21.20	+ 0.49	−12.61
Providence	21.42	21.36	18.13	− 0.28	−15.12
Richmond	20.72	20.26	19.27	− 2.22	− 4.88
Rochester	12.62	13.90	15.40	+10.32	+10.79
St. Louis	16.86	16.44	14.03	− 2.49	−14.66
St. Paul	21.70	19.58	18.43	− 9.77	− 5.88
San Francisco	12.30	12.16	9.83	− 1.14	−19.16
Seattle	15.14	14.94	12.43	− 1.32	−16.80
Toledo	16.70	16.62	15.53	− 0.47	− 6.56
Washington	19.38	17.66	14.43	− 8.87	−18.29

The figures in Table No. 1, although those most employed, are not absolutely fair for comparative purposes, as cities vary greatly in their per cent. of population at this age period.

Table No. 2, showing the per cent. of deaths under one year of age to each thousand births, would be the fairer method, if it did not depend upon the completeness of birth registration, which in some places is far from satisfactory, it being estimated in one of our large cities that less than 50 per cent. of all births are recorded.

TABLE 2—DEATHS OF INFANTS UNDER ONE YEAR OF AGE PER 1000 BIRTHS

Cities.	1900.	1910.	1912.	1914.
Atlanta	258.8	213	—	—
Baltimore	208.5	218	177.7	154.6
Boston[1]	173	126	119	103.4
Buffalo[1]	137	162	127	121.5
Chicago	134	281	—	132.7
Cincinnati[1]	155.3	131	103	—
Cleveland	163.6	150	137	118.4
Denver	146.6	163	—	—
Detroit[1]	176.5	179	132	122.4
Indianapolis[1]	153.7	123	101.5	102.2
Jersey City	175.6	204	149.8	105.1
Kansas City, Mo.[1]	165.1	154	166.8	—
Louisville	155.6	145	108	—
Milwaukee[1]	167.6	145	—	—
Minneapolis	95.2	109	72.4	82.7
New Orleans	197.9	162	102.3	112.2
New York[1]	170.5	125	105.3	94.4
Newark[1]	164	124	—	—
Philadelphia[1]	178	138	102.4	117.6
Pittsburgh[1]	162.1	150	126.7	115.2
Providence[1]	190.2	144	112.7	112.7
St. Louis[1]	146.3	115	97.3	103.4
St. Paul	91.2	132	96.1	97.5
San Francisco	136.2	108	100	—
Washington, D. C.	232.7	152	128	—

The relation of mortality to the number living at the same age therefore seems to be the fairest method of comparison with the means we have at our disposal, and is shown in Table No. 3.

The best work now being done is in a city appropriating the largest sum per capita of population of any of the large cities to the health department, which tends to bear out the quotation appearing upon their official publications: "Public health is purchasable. Within natural limitations a community can determine its own death-rate."

Not until after the National Conference for the Reduction of Infant Mortality held in London in 1906, were efforts to reduce infant mortality thoroughly organized. This conference caused a general awakening, and was followed by the formation, at first

[1] Cities where the reported number of births exceeded the population under one year of age by 10 per cent. or more, and therefore the ratio of infantile mortality given is probably approximately correct. The figures for 1900 and 1910 are taken from the United States Census reports. The figures for 1912 and 1914 are obtained from local health officers.

local, of associations in both Europe and America. These have continually increased in both number and influence, until today there are but few communities not realizing "that the great infant mortality is a national disaster," which constitutes the surest index of inefficiency of health administration, private and public.

TABLE 3—DEATHS UNDER ONE YEAR OF AGE

Cities.	Average per cent. of deaths to those living. 1901 to 1905.	1906 to 1910.	1911 to 1913.	Per cent. change. 1906 to 1910 from 1901 to 1905	1911 to 1913 from 1906 to 1910.
Baltimore	22.36	22.18	19.73	− 0.80	−11.05
Boston	17.26	17.81	15.82	+ 3.18	−11.17
Buffalo	15.10	17.63	16.07	+16.76	− 8.85
Chicago	12.72	13.97	13.07	+ 9.82	− 6.44
Cincinnati	15.92	15.58	12.70	− 2.14	−18.49
Cleveland	15.81	14.65	12.37	− 7.34	−15.57
Denver	14.18	14.67	11.07	+ 3.46	−24.54
Detroit	15.73	18.33	18.33	+16.53	0.0
Indianapolis	15.48	13.48	11.53	−12.92	−14.46
Jersey City	17.65	16.70	13.03	− 5.38	−21.97
Kansas City, Mo.	15.76	15.26	15.22	− 3.17	− 0.26
Louisville	17.07	14.31	12.33	−16.17	−13.84
Milwaukee	14.22	16.32	15.80	+14.77	− 3.19
Minneapolis	7.90	9.54	10.07	+20.76	+ 5.56
New Haven	15.38	14.42	12.57	− 6.24	−12.83
New Orleans	17.53	16.98	13.20	− 3.14	−22.26
New York	16.65	15.68	12.50	− 5.83	−20.28
Newark	15.06	14.66	11.80	− 2.66	−19.51
Philadelphia	16.04	17.10	13.37	+ 6.61	−21.81
Pittsburgh	18.25	17.32	13.80	− 5.10	−20.32
Providence	19.24	17.83	13.30	− 7.33	−25.41
Richmond	21.82	20.26	18.23	− 7.15	−10.02
Rochester[1]	9.42	10.85	12.30	+15.18	+13.37
St. Louis	15.44	13.90	12.00	− 9.97	−13.67
St. Paul	11.13	12.02	11.50	+ 8.00	− 4.33
San Francisco	16.22	13.16	10.57	−18.87	−19.68
Washington	23.54	20.86	15.87	−11.38	−23.92

The further study of the development of infant welfare work in the United States shows that the initiative, without exception, has been taken by private interests. Where these interests were successful and accomplished results, in a majority of instances through the education of the public, the municipal authorities were induced to recognize their full duties, and organize bureaus or divisions of "child hygiene." In most cities and states, this

[1] Returns to Census Bureau incomplete, considerable number of deaths omitted.

activity properly falls under the health department, but in the United States government is under the Department of Labor.

Municipal departments of child hygiene were organized first in New York in 1908, then in Philadelphia, Chicago, Detroit, Los Angeles, and Buffalo in 1910, in Boston, Cincinnati and Kansas City, Mo., in 1911, Milwaukee and Cleveland in 1912, followed later by Newark, Indianapolis, Rochester, Seattle, Providence, and others.

State control was given by Act of Assembly of Pennsylvania approved April 27, 1905, creating a state department of health. Under this power child welfare exhibits have been held, much circularization done, and organization of medical school inspection accomplished. In 1913 a law was passed by the New York legislature creating a division of child hygiene in the State Department of Health, as the result of the report of the special commission appointed by the governor in January, 1913, to make recommendations "as to changes in the public health laws" which was embodied in the governor's message to the legislature February 19, 1913; and among other things, advised that "each city with a population in excess of 10,000 and having an industrial population, should have one infant welfare station, and larger cities with an industrial population should have one such station for approximately each 20,000 inhabitants."

A division of child hygiene was created in the Kansas State Board of Health by Act of Assembly approved March 6, 1915, providing among other things that the "general duties of this division shall include the issuance of educational literature on the care of the baby and the hygiene of the child, the study of the causes of infant mortality and the application of preventive measures for the prevention and the suppression of the diseases of infancy and early childhood, and such other duties as are prescribed by the State Board of Health."

The United States government at a late date took cognizance of the importance of this subject, and by Act of Congress approved April 9, 1912, created a Children's Bureau in the Department of Labor to investigate "all matters pertaining to the welfare

of children and infant life." This bureau collects information for publication. It has already issued pamphlets on "Birth Registration," "Aid in Protecting the Lives and Rights of Children," "Baby Saving Campaigns," "Pre-natal Care," "Infant Care," "Handbook of Federal Statistics," "Infant Mortality," "The Results of a Field Study in Johnstown, Pa., Based on Births in One Year," "New Zealand Society for the Health of Women and Children," and "An Example of Methods of Baby Saving Work in Small Towns and Rural Districts."

It acts as a clearing house for all private, municipal, and state agencies, through which information on any phase of infant welfare work is imparted, and endeavors to stimulate local interest in communities where it is most needed.

The only other national government activity is the Public Health Service, which has published at various times reports on "Milk Stations," a report of the "National Commissions of Milk Standards" and a booklet on the "Care of Children" compiled by the American Association for the Study and Prevention of Infant Mortality.

The first generally organized conference in this country on the prevention of infant mortality was held by the American Academy of Medicine at Yale University, November, 1909, out of which grew the American Association for the Study and Prevention of Infant Mortality, which has carried on the work:

"Through studies and investigations by special and standing committees;

"Through annual meetings, the transactions of which form practically a year book on the subject;

"Through a campaign of education, by the publication and distribution of material on the subject; by correspondence from the home office, which as far as possible has served as a medium for the exchange of information on the part of the organizations engaged in baby-saving work, or planning to do so; by use of the travelling exhibit."

Among the earliest municipal activities may be mentioned: The Good Samaritan Dispensary of New York, 1891; The Pasteur-

ized Milk Stations of Nathan Strauss, 1892; Milk Stations in Rochester, New York, 1897; Milk Fund Association, Cleveland, 1899; commencement of child hygiene work by the Department of Health, New York City, and the Philadelphia Modified Milk Society, Philadelphia, 1903; Babies' Milk Fund Association, Baltimore, and the St. Louis Pure Milk Commission, St. Louis, 1904; Poor People's Modified Milk Service, Boston, Association for Improving Conditions of the Poor, New York, and the Chicago Milk Commission, 1905; Babies' Dispensary and Hospital, Cleveland, and Committee on Modified Milk Stations, Boston, 1906; and Louisville Babies' Milk Fund Association, Louisville, 1908.

Up to this time nearly all work had been concentrated on providing a pure milk supply for infant feeding, as diarrhea and enteritis, constituting the greatest preventable menace to infant life, until recently, was believed to be entirely caused by rapid deterioration of uncooled or improperly kept milk, especially in in hot weather. The mortality rate in the United States from these diseases was but little affected until after 1910, although local efforts to improve the milk supply showed results in certain communities prior to that time, as shown in Table No. 4.

Improvement and efficiency has been marked from year to year, showing progress from the earliest effort to improve the milk supply, until the following activities are now incorporated in most well equipped health centres controlling infant life.

Milk. Milk stations were primarily established to provide milk of good quality for infant feeding, for which mothers and care-takers were compelled to call. Later, milk was delivered to the house, at cost, below cost, or free. In the latter case the expense was borne in many cities by private relief agencies. It took but little practical experience to demonstrate that the provision of a pure milk supply was of but little benefit if the milk was improperly kept after its receipt in the home, so the education of the mother and care-taker became most important, and the visiting nurse was added to the milk stations for this purpose. Then physicians were employed to advise mothers how properly to care for sick babies.

TABLE 4—DEATHS FROM DIARRHEA AND ENTERITIS UNDER TWO YEARS OF AGE PER 100,000 OF POPULATION

Cities.	5-year averages. 1901 to 1905.	1906 to 1910.	3-year average. 1911 to 1913.	Per cent. change. 1906 to 1910 from 1901 to 1905.	1911 to 1913 from 1906 to 1910.
Baltimore	129.4	118.0	99.1	− 8.8	−16.0
Boston	107.4	99.2	87.9	− 7.6	−11.4
Buffalo	112.0	139.7	127.2	+24.7	− 8.9
Chicago	104.4	138.0	137.9	+33.2	− 0.7
Cleveland	104.0	132.4	135.6	+27.3	+ 2.4
Cincinnati	77.7	86.2	65.6	+10.9	−23.9
Denver	47.4	55.1	30.6	+16.4	−44.4
Detroit	99.6	102.8	101.2	+ 3.1	− 1.5
Indianapolis	48.1	68.4	51.8	+42.2	−24.3
Jersey City	125.9	142.7	95.6	+13.3	−33.0
Kansas City, Mo.	46.1	45.7	68.6	− 0.9	+50.1
Louisville	50.2	37.9	33.6	−24.5	−11.3
Milwaukee	95.9	119.0	100.1	+24.1	−15.9
Minneapolis	41.9	55.8	37.7	+33.2	−32.4
New Haven	110.0	91.7	68.4	−16.6	−25.4
New Orleans	113.8	130.3	109.7	+14.5	−15.8
New York	145.0	133.8	82.9	− 7.8	−38.1
Newark	106.5	112.9	104.0	+ 6.0	− 7.9
Philadelphia	96.8	133.5	104.0	+37.9	−22.1
Pittsburgh	170.2	169.1	126.2	− 0.6	−25.3
Providence	134.7	120.2	73.1	−10.7	−39.2
Richmond	127.2	133.6	116.3	+ 5.0	−12.9
Rochester	51.6	82.6	87.9	+60.0	+ 6.4
St. Louis	62.8	73.7	76.4	+17.4	+ 3.7
St. Paul	43.7	58.0	45.4	+32.7	−21.7
San Francisco	57.7	47.1	37.3	−18.4	−20.8
Washington, D. C.	118.8	99.0	66.0	−16.6	−33.3

Clinics. Clinics were thus established with daily service, in some cities, during the hot weather, in others during the entire year. The education of the mother became of more and more importance, so that demonstrations, lectures, and distribution of literature were added features of the medical dispensaries and clinics, so they then in reality became,

Welfare Centres. Welfare centres, of which there were in 1914 a record of forty-three in thirty different cities of over 50,000 population, twenty-nine of which were supported by private benevolence. Dr. Philip Van Ingen of New York, in a recent article, stated he had data "concerning 204 such centres in thirty-nine cities."

Visiting Nurses. The visiting nurse is the most important function in the reduction of infant mortality. In most cities a

nurse is sent to all tenements and poor districts upon receipt of information of a birth or expected birth. Subsequent visits are not made without the consent of the mother, attending physician, or midwife. The nurse gives instruction in child hygiene, care of the baby, general sanitation and the importance of breast-feeding.

Dr. Josephine Baker, Director of Child Hygiene in New York, in an argument for additional nurses, demonstrated that "babies can be kept under continuous home supervision at a cost of sixty cents per month per baby, as compared with two dollars per month per baby under care of milk stations." She further says "the solution of the problem of infant mortality is 20 per cent. pure milk and 80 per cent. training of the mothers. The infant milk stations will serve this wider usefulness when they become educational centres for prenatal instruction and the encouragement of breast-feeding and teaching of better hygiene, and the mothers instructed to buy the proper grade of milk at a place most convenient to the home." The proper home care of infants by their mothers in relation to mortality is forcibly demonstrated by the experience in Lowell, Mass., and Paris; in the former city during an extended labor strike in the mills, women could not work and perforce were compelled to remain at home and nurse or give constant care to their children. During this period infant mortality decreased, while the general mortality, as a result of privation and poverty, increased. And in Paris, during the siege in the Franco-Prussian war, when opportunity for outside work was cut off, and women were compelled to remain at home, the general mortality doubled, while infant mortality fell off 40 per cent.

Housing and Sanitation Bad housing and sanitation bears directly on infant mortality. A large number of diseases are produced by conditions coming under the head of bad housing. Lack of cleanliness, bad ventilation, poor light, bad drainage, etc., are being combated by the visiting nurse, but the abatement of nuisances must be accomplished by public health officers, who, in a few communities, have been ably assisted by local and private housing commissions, and the National Housing Association,

whose efforts in improving the condition of the poor, and the lowering of mortality, have been demonstrated where their activities have been most needed.

Midwives. The supervision and control of midwives are under state and municipal government in many parts of the country. In thirteen states, midwives are allowed to practice without restraint, and in fifteen others, there is no control or requirement for training or licensure. In some cities where examinations for licensure are required, schools for instruction have been started; for example, New York operates a school in connection with the Bellevue Hospital; in Philadelphia a similar course has been inaugurated in connection with the Philadelphia General Hospital and the Preston Retreat, and continued until 1913, when the control of midwives was taken from the Bureau of Health and vested in the "State Board of Medical Education and Licensure" by Act of Assembly.

Day Nurseries. Day nurseries are very numerous. They provide daily care for babies and children, and although some are most worthy charities, yet others are insanitary, poorly managed, and productive of harm. These nurseries are rarely under municipal control.

Little Mothers' League. Little Mothers' Leagues, inaugurated in many cities, have awakened great interest in the care of infants, and are today an important feature in imparting knowledge in the home, and eventually will prove of inestimable value in the improvement of the future race as these young girls become mothers. Classes of girls are formed, generally in connection with the public schools. Lectures and demonstrations on the care of the baby are given by physicians and nurses. In many cities examinations are held and medals or other insignia are awarded at the end of the course to those who have put their knowledge to the best practical use.

Boarding Out Infants. The municipal supervision, in many cities, of the boarding out of infants has been important in bringing under control the so-called baby farms, which have frequently been in the past an important feature in increasing infant mortality,

in encouraging immorality, and the deserting of babies by their parents.

Education and Publicity. "Philadelphia is the first city to teach the vocation of motherhood to girls in public schools as part of their curriculum." This instruction was made part of the Domestic Science course by the Board of Education in 1914.

The Western Reserve University of Cleveland has recently added to the curriculum of the senior class of the Medical School eight hours for the study of "Practical Training in Social Medicine Pertaining to Infant Welfare Work." The importance of this can be attested by Civil Service examiners, who have noted the lack of knowledge in this particular branch of hygiene on the part of physicians taking examinations for interneships in hospitals and various positions in public health service.

Among the first to use publicity in the campaign for child welfare were Nathan Strauss, of New York; the *Delineator;* the Russell Sage Foundation; the Metropolitan Life Insurance Company, and a few other private agencies. Special note should be made of the work of the Metropolitan Life Insurance Company, as great impetus, irrespective of motive, has been given publicity by their work of recent years. Much good has been accomplished through the issuance of a book called *The Child*, over three million copies of which have been distributed by the physicians and agents of this company to its policyholders. This publication was followed by a pamphlet on "Milk and its Care," written by Professor Rosenau. Nurses are provided free for the care of the sick, and educational work in over seventeen hundred cities and towns. The company, moreover, offers its services to all health officers.

Publicity by municipal departments has been obtained through circularization, milk stations, settlement houses, libraries, public schools, visiting nurses, medical inspectors, policemen, posters with printed instructions and pictures sufficiently attractive to find lodgment on the walls of the home, and newspapers, most of which have generously opened their columns for the education of the public in their own betterment.

Baby Contests. Baby contests have been held for publicity purposes in many of our large cities, frequently under the auspices of some particular newspaper which has awarded prizes for improvements shown, and thereby added much to the public interest.

Exhibits. Exhibits have proved among the most instructive form of publicity. In cities like New York, Chicago, and Philadelphia, they have been very elaborate and largely attended. The results obtained demonstrated the importance of this feature of the work to such an extent that the American Association for the Study and Prevention of Infant Mortality prepared a travelling exhibit first shown at the International Congress of Hygiene in Washington in 1912, when it was awarded one of the few diplomas of special merit. This exhibit has been in the field ever since and has been shown in twenty-eight cities. "The actual showing of this exhibit has been represented by but a small part of its usefulness. It has served as a basis for a number of exhibits," which have been adopted by many boards of health, a number of universities, chambers of commerce, and other associations. Complete photographic sets of the exhibit, together with circulars of explanation and instruction have been furnished many organizations.

Floating Hospitals. Floating hospitals have been in use in certain localities. The best illustration of their efficiency is in Boston where this open-air service was established and is maintained by private subscription. A large steamer leaves the wharf at nine o'clock in the morning during the heated term, cruises or anchors in the harbor, and returns at five o'clock in the afternoon. A sufficient number of physicians and nurses are in attendance to care for two hundred children per day. This is a worthy charity, but expensive. It is believed that the same amount of money spent in a more practical manner would give better results.

Prenatal Work. Mortality during the first year of life in all registration cities of the United States has been decreasing. In 1909 this mortality was 22.31 per cent. of the total mortality; in 1910 it was 19.95 per cent. and in 1913, 17.9 per cent. Yet a careful study of vital statistics shows that the number of deaths

under one month of age has been continually increasing up to this period and especially during the first days of life; showing that efforts already exerted for the prevention of infant mortality, although successful for later age periods during the first year, did not affect this early mortality, due to causes acting before birth; and concentrated attention upon the importance of prenatal work which, during the recent past, has become more prominent and today plays a large part in the campaign to combat infant morbidity and mortality, the result of which is beginning to appear in our vital statistics.

Table No. 5 shows the comparison of mortality in cities and rural districts for various age periods under one year for 1910 and 1913.

TABLE 5—DEATHS BY AGE PERIODS, UNDER ONE YEAR IN THE REGISTRATION AREA OF THE UNITED STATES

Age.	All registration cities.		Rural parts of registration states.	
	1910.[1]	1913.	1910.	1913.
Less than one day	10,614	11,694	6,573	9,668
One day	5,254	4,401	3,380	3,350
Two days	3,174	3,094	1,947	2,284
Less than one week	25,372	25,326	16,071	20,006
One week	6,284	5,680	3,956	4,543
Two weeks	5,150	4,221	2,920	3,273
Less than one month	41,420	38,692	25,392	30,285
One month	11,597	8,816	5,910	6,096
Two months	9,754	7,410	5,107	4,815
Three to five months	22,832	16,960	10,443	10,734
Six to eight months	16,828	12,637	8,209	7,259
Nine to eleven months	12,798	9,939	6,249	5,792
Under one year	115,220	94,454	62,309	64,981

Here again there is a possible source of error, for in order to secure accuracy, we must assume that the same relation in increase of population holds for all age periods. In the cities a marked reduction has taken place in every age period, excepting under one day, demonstrating most forcibly the necessity for increased research work and study of prenatal conditions responsible. In the rural districts the mortality in 1913 in nearly all age periods shows an

[1] As the registration area of the United States in 1910 included 58.3 and in 1913, 65.7 per cent. of the population, an actual difference of population of 9,454,822 (15 per cent.), it would be impossible to make a fair comparison without the correction of the 1910 figures which has been done.

increase, amounting to 4 per cent. in the total deaths under one year; while for the same time in the cities there is a decrease of 18 per cent. As but little effort in infant welfare work has as yet been made in the rural districts, the result is as expected, and places the credit for the reduction in this mortality to the campaigns waged in the cities. The earliest systematic prenatal work has been done in New York, Cleveland, Philadelphia, Boston, St. Louis, Chicago, Baltimore, and some of the smaller towns, of which Fall River, Mass., may be specially noted.

A synopsis of the work in a few of our large cities will serve to show the varied methods adopted in different locations.

New York. In 1891 milk was dispensed in the summer to sick babies by the Good Samaritan Hospital. In 1892 Mr. Nathan Strauss founded pasteurized milk laboratories in various parts of the city. In 1903 the Health Department appointed physicians and nurses to visit families of newborn babies. In 1905 The New York Association for Improving Conditions of the Poor entered into a vigorous campaign for clean milk, which movement was initiated by the Commissioner of Health. In 1906 the New York Milk Committee, supported by private means, was formed to investigate the entire milk problem, and within two years engaged in active field work by installing milk depots and employing nurses to do instructional field-work in connection therewith. They encouranged breast-feeding, and educated the mother in the care of the infant, and did experimental work to compare results "obtained by the continued use of pasteurized and of raw milk to determine" which was the more economical and satisfactory method of saving infant lives. The work of this committee and of Nathan Strauss has been largely instrumental in the pasteurization of ordinary market milk now required in many of our cities. In 1908 the Division of Child Hygiene in the Department of Health was organized with a chief, five assistant chiefs, sixteen supervising inspectors, one superintendent of nurses and one hundred and ninety-five district nurses. In 1909 the division took under supervision midwives, boarding places for children, day nurseries, and other institutions for the care of children. In this year Little

Mothers' Leagues were started in the public schools, and in 1910 appropriations were increased sufficiently to maintain fifteen infant milk depots. In the same year twenty-three additional milk stations were opened in New York, and in 1911, an Association of Infant Milk Stations was formed to prevent duplication of work and bring the eight existing organizations, maintaining seventy-five stations, under central control.

Philadelphia. Although some desultory and individual effort had already been exerted, the first organized movement was by the Philadelphia Modified Milk Society in 1903. Modified milk under various formulæ was delivered to mothers calling at the various stations in different parts of the city. In the spring of 1907 the Department of Public Health and Charities organized volunteers from various churches into committees on visitation of homes of young mothers. Philadelphia was first in the field to organize clinics for the treatment of poor school children. In 1908 an eye clinic, and in 1910 a dental clinic was established in the Bureau of Health. Prior to this time dental work had been performed in private institutions made possible through appropriations by councils for this purpose. In 1908 The Babies' Alliance was formed, to extend the work already started in every ward in the city, and to carry on a publicity campaign by circulars, bulletins, baby contests, Little Mothers' Leagues, and the newspapers. There was inaugurated in 1909 an aggressive campaign against the use of soothing syrups and other proprietary medicines, which received the official support of the Retail Druggists' Association of Philadelphia. Classes of mothers were held once a week in different sections of the city, and prizes were given by the Babies' Alliance and Light House to mothers for those babies showing the best results. A novel feature of education was introduced at this time by the Bureau of Health, consisting of large paper bags, upon which simple instructions to mothers were printed and placed over every bottle of milk sold. Every milk pitcher or can left on the door-step for milk was also covered with one of these bags. The latter served the double purpose of distributing information and preventing contamination of milk

served loose. The success of this movement was made possible by the hearty coöperation of the milk dealers. In 1910 the Philadelphia Conference on Summer Work for Mothers and Children was started. It secured the coöperation of one hundred and fifty-seven private associations, covering day nurseries; settlement and neighborhood houses; social betterment agencies having facilities such as baths, camps, mothers' clubs, milk stations, etc.; agencies providing temporary shelter for mothers and children; modified milk stations; hospitals and dispensaries; associations providing convalescent care or outing; agencies visiting and inquiring into the needs of mothers and children in their homes; and the various bureaus of the City Department of Public Health and Charities. This work, although financed privately, was conducted under the auspices of the City Department. The Philadelphia Modified Milk Society added milk stations, the Bureau of Municipal Research supplied one clerk and two nurses, the Phipps Institute, one, and the Starr Centre, two nurses. Work started May 1, and the publicity obtained proved sufficient incentive to have the municipal legislative body immediately appropriate sufficient money to employ one supervising nurse and eight visiting nurses, which constituted a commencement of a division of child hygiene. The district physicians and medical inspectors of the Bureau of Health were employed in this division during the summer recess of the public schools. A milk station, a clinic, an exhibit where lectures were given daily, were established on one of the city piers, and a hospital for sick babies on another. All requests for medical or nursing aid could be, day or night, forwarded to the central office in the Bureau of Health through the police or fire station houses, by telephone. Bulletins, posters and circulars were distributed largely through the police department. In 1911 an elaborate milk show was held at which the attendance was 110,681. In an adjoining auditorium, lectures and moving pictures were given daily. A commission was appointed by the mayor in 1910 to study the entire milk problem. An elaborate report was published February 15, 1911, which aided materially in securing public endorse-

ment of improved rules and regulations authorized by Act of Assembly, approved April 27, 1909, which finally brought the milk supply of the city under the control of the Department of Public Health and Charities.

A Child Hygiene Committee was organized in 1911 which, in coöperation with the city health authorities, held a large Baby Saving Show visited by 67,507 people. Lectures and moving pictures were a daily feature. The benefit derived from this show was so great that it was converted into a travelling exhibit, and has been almost continuously used in different parts of the city. During the year 1913 alone the attendance was 351,860. The Child Hygiene Committee changed its name in the year following to tbe Child Hygiene Association, which on September 30, 1913, incorporated under the title Child Federation, "to actively advance by original and constructive methods the best interests of babies and children in Philadelphia." They turned over to the Board of Education the Little Mothers' Leagues, and secured the introduction of the course on child hygiene in the public schools, as already noted. In 1914, through the efforts of this Federation, the Babies' Welfare Association, consisting of eighty-four various activities partly engaged in similar work, was organized to prevent duplication of labor by coördination and coöperation; thereby creating a central supervision of the various associations, and becoming a clearing house for all interested in child welfare work, with a central office in the Bureau of Health. Committees were appointed to do special research work, the effect of which is already felt in the creation of most effective health centres, the better control of baby farms, lying-in establishments, milk stations, and day nurseries.

Cleveland. The first effort to reduce infant mortality was made in 1902 with the formation of the Milk Fund Association which supplied modified milk to babies who were brought to the office of the Association. On July 5, 1906, the Visiting Nurse Association, an organization sending nurses into the homes of the sick, effected a coöperation with the Milk Fund Association. In December of the same year, the Babies' Dispensary and Hospital

was incorporated, which, at a later date, took over the already existing organizations and opened in May, 1907, a dispensary in a converted frame building on property purchased, where both sick and well babies were brought. As the work increased, dispensaries were opened from time to time in various portions of the city, until 1908, when there were eight, for which the central office acted as a clearing house. In 1910 permanent buildings were erected for a central dispensary and milk laboratory. Through practical work and a publicity campaign, city councils in 1911 appropriated ten thousand dollars to the Board of Health for infant mortality work, making the Babies' Dispensary advisors to the Board "in the manner of application of funds," and ended in establishing a department of child hygiene in the Board of Health, with the medical director of the Babies' Dispensary and Hospital as director thereof. In 1912 all the dispensaries of the private associations were turned over to the municipal department, so that all the prophylactic work was conducted by the municipal government and the care of the sick by the Babies' Dispensary and Hospital.

It is impossible to cover all details that have a bearing on the progress of recent public health work, but the foregoing history of a few of our cities is a fair exposition of the methods employed in infant welfare work. The results of these methods are found in a careful study of vital statistics. Notwithstanding the great progress, it is well known that but a beginning has been made, as the field of opportunity is ever broadening and new problems constantly arise, that at the time appear almost insurmountable.

Let us trust the results already obtained may prove an incentive to renewed efforts that, in view of past experience, will undoubtedly place in the list of preventable deaths, prematurity and congenital debility, which now exact such a toll during the first few days of life.

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DISCUSSION

Dr. A. C. Abbott: I think you must have been impressed, as I have, with facts brought out by these papers to the effect that public preventive medicine has a social bearing that is quite as obvious as its medical.

It is indeed refreshing to participate in a discussion along lines other than purely medical in this College.

Dr. Neff has so fully covered the details of his special field, and has brought out so lucidly what is being done in that field that I scarcely feel his paper requires discussion.

In Dr. Ferrell's address, he has discussed one of the biggest economic propositions we have seen. It is startling to realize that in an area of 30 degrees north and south of the equator, and encircling the world, there resides a population of about 100,000,000 people, approximately 90 per cent. of whom are suffering from parasitic ailments that rob them of their efficiency. We know that the most important of these parasitic ailments are easily curable, and I trust you realize what it will mean to restore this horde of people to health and earning capacity.

To bring the matter more nearly home, I would remind you that the survey made by the Rockefeller Foundation of eleven of our own Southern States, with a total population of more than 2,000,000 of people, reveals

a like condition. Many of these people are incapable of effective work, and thousands of the children are unable to profit by the education that is offered them. I believe the conditions revealed by the Rockefeller survey are in a large measure accountable for the restrictions on progress in the South.

With these thoughts in mind, I think you can realize the importance of the International Health Commission's efforts to restore these people to health. In the several reports of the commission we find that in some of the States embraced within the survey not only is there an enormous number of adults infected, but the majority of school children and many teachers were found to be harboring the parasite that exists only by sucking the life blood of its host. You can easily understand that such conditions constitute a terrible handicap against intellectual and material advancement. It is fortunate that the disease is easily cured and that in the majority of instances it leaves behind it no structural defects likely to interfere with a person's earning capacity. As I said above, restoration to efficiency of this large part of our population must be looked upon as of the greatest economic importance to the part of the country in which they live.

I am optimistic, and I believe the movements begun by the Commission will be extended to other tropical diseases and will be rewarded with success. It is the tropics that offer to us our great field for sanitary activity. I am delighted that Dr. Ferrell has given us a chance to hear of the work of the International Health Commission, and I believe I speak for the College when I say that everything that lies in our power to forward that work will be gladly done.

Dr. S. Lewis Ziegler: I am very much interested in these problems from the two different stand-points presented by Dr. Ferrell and Dr. Neff—the hookworm problem in the South, and baby welfare in the northern part of the country. I think Dr. Abbott has struck the keynote of the subject in the question of economy to the country at large, and that is the argument we have to use in order to secure funds to forward this movement.

The problem put before me not long since by the Subcommittee of Finance of this city was that the Department of Public Health and Charities was asking for $78,000 for the mere purpose of taking care of babies; and, not withstanding the fact that I called attention to the fact that there had already been appropriated $38,000, the difference of $40,000, so far has not been forthcoming. In the budget put out a few weeks ago the part for child hygiene was omitted.

There seem to be several obstacles to progress along these lines. The first is that of selfish interests. Take the question of housing, in which

is seen the selfish interest of the owner in not wanting to add proper sanitary appliances because of the expense. The second proposition involved is that a lot of political appointments are liable to be brought about by the Housing Bill, and it is opposed on that account. A third proposition, so far as the legislator is concerned, is the question of "ego." There is the idea that someone is trying to force something on him and he will not consent. The only thing that will bring about progress is a united community. I think anyone thoroughly convinced of the right of a question in which human life and health are involved will yield and grant that which is necessary. That is the problem which will come up tomorrow in connection with the hearing before the governor on the Housing Bill, whether or not the community will support a good housing law. The diversified interests of the Department of Public Health reminds one of the Colossus of Rhodes, with one foot in Philadelphia and one in Harrisburg, but standing on tip-toe with a wire attached to each one of the toes.

The question of child hygiene is very close to all of us, and no one has done more in that direction probably than Dr. Neff.

Dr. Furbush has also given much time and attention to this subject, while Mr. Bok and Mr. Cross have shown deep interest in this humane undertaking. This problem is so vital to the community that we should make every endeavor by action and public expression to demonstrate that our aims are simply humane and altruistic, and that our sole purpose is to bring about the greatest good to the greatest number.

Dr. J. C. Gittings: I regret very much not to have heard all of the papers, but could add very little to the discussion. It seemed to me that I might emphasize several points about the infant welfare movement, especially as it applies to Philadelphia.

First, that ignorance, and not poverty, is the chief factor in causing infant mortality. Second, that the properly selected and properly trained nurse, acting under competent supervision, who serves as educator, adviser, and counsellor of the poor in matters concerning health, is the logical cure for this mortality. Third, that the crying need in Philadelphia is for the enlargement of the division of the bureau of health devoted to child hygiene and the employment of an adequate number of nurses.

The chief causes of infant mortality in cities are: I. Overcrowding. II. Improper housing. III. Filth and poor hygiene. IV. Improper food. On analysis we find that ignorance, much more than poverty, sets these causes into play. For example, overcrowding and poor housing are economic in the sense that parents cannot afford better quarters, but often the baby suffers from the parents' ignorance of their evil effects. When they are better educated, they will move—an argument which

may prove very efficacious in securing better housing conditions. It is perfectly clear, also, that knowledge means power through the ballot which can correct many existing defects. Improper food usually means, for the baby at least, improper preparation of food, which is chiefly due to ignorance, while filth and poor hygiene can be almost eradicated by proper education. It was this recognition of the importance of ignorance in the causation of infant mortality which formed the mainspring of the greatly increased activity of recent years in work for the infants' welfare. Of all the proved agents for medical sociologic relief, the sociologic nurse, as she might be called, is the most efficacious, and this is particularly true with regard to the care of infants. A series of evenings would be required to demonstrate the potentialities of the sociologic nurse in dissipating the dense clouds of ignorance and superstition which envelop and hamper the mother of the poor in her care of the baby. Hospitals and other agencies are employing the function of the nurse more and more in their social service work, but they are only scratching the surface of the vast field of need. The ultimate outcome of the movement involves the municipality itself. The Department of Health is doing all that is possible with the appropriations at hand, but the chief need is for fund to employ an adequate number of nurses. There are not a few physicians who are inclined to view the attempt to alleviate conditions in the slums as more or less Utopian, but the greatest stumbling block in securing the acceptance of the larger program of municipal relief lies in the inertia of the lawmakers. Their attitude in public-health measures always is Missourian—they must be shown the necessity for them, and especially they must be convinced that the public, as a whole, approves and demands them. This is natural enough from their standpoint, and shows the need for education of the public itself as well as the law-makers.

To both the doubtful ones among the profession and to the law-makers one can only say that when we note the extent to which the infant welfare work has reached—when we stop to realize the character and capabilities of the men and women who are making it their life-work and study and when we see the tangible results in the reduction of infant mortality, even the greatest skeptic must admit that the movement has passed far beyond the experimental stage, that it can no longer be classed as an idealistic dream of the millenium, but a demonstrated feasible measure for saving human life which has an almost infinite range of possibilities, directly dependent upon the aid and support which it receives from the municipality.

Dr. Randle C. Rosenberger: Infantile mortality, whether it is due to direct injury of the infantile organism by hot weather under unfavorable nutritive and living conditions; or, whether it is an infectious

disease, or only a disease of the intestinal tract caused by the food which so easily decomposes in children, is a most vital question in child welfare.

We must not forget to care for the mothers, because we will find most of the mothers whose children are ill and die from summer complaint are poor, poorly nourished, and do hard, manual work even up to the day of the birth. Care and want and worry harass the illegitimately pregnant female, and these conditions no doubt play a part in the defective development of the child.

Could it be possible that pregnant women be excluded from occupations injurious to health, and rest given to the mother before birth, or, as is at present established in France and Germany, an adequate law which protects the mothers against want during pregnancy and the puerperal state—by financial aid up to six weeks, nursing money to the twelfth week, and medical aid given, it would be a glorious undertaking. It is claimed that in France since the establishment of this social institution of motherhood insurance the mortality of infants has decreased by 50 per cent.

It is a well-known fact that not only poverty and want rob the child of its natural nursing fount, but that luxury, pride, vanity, false notions, and frivolity are the motives which repress the highest of motherly duties.

To this end the mother should be encouraged by education, or by nursing premiums in the form of money, food, or boarding institutions.

Education as regards the care of the child should be insisted upon, because even in the well-to-do, children perish because of a lack of any knowledge of child care.

It should be impossible for a girl to become a mother without having the least idea how to rear, feed, and care for a baby and how to protect it from disease.

A course could be given to girls on the care of children and child hygiene which would abundantly fit them to become teachers or mothers themselves. (Bodily cleanliness; bathing and clothing; knowledge of nutrition; care of milk bottles; clean milk; quantities of food; protection against underfeeding and overfeeding; types of food; necessity of sleep; fresh air; dangers of infection; consideration of children's diseases; reëducation out of false notions; superstitions concerning care of children; false belief in danger from teething; belief in the evil eye; charms against it, wearing of amulets, etc.)

Consider the great economic value to the commonwealth if these conditions should come to pass in the great number of well-developed, healthy, and efficient citizens who probably would have perished if not properly taken care of when young.

The helpless child must then be further looked after by legislation and

by social endeavor. The Taube system—in the care of illegitimate children—the appointment of a legally constituted authority (legal guardian), compelling the father to do his duty and care for the child.

Too much credit cannot be given the social service workers who have done noble, heroic work with the limited means at their disposal—sacrificing time and household duties in trying to benefit the poor, helpless unfortunates who are constantly being brought into the world.

As the child matures and develops evil influences, especially in cities, make their appearance in the crowded dwellings, lack of sunlight, lack of open spaces or parks or recreation grounds, public baths, dangers of contagious diseases in schools and homes; overwork; immediate exposure to the use of alcohol and sexual indulgence. We should also consider the erection of hygienic and sanitary schools, open-air sanatoria, recreation parks, swimming pools, regulation of child labor.

Further, there should be a coöperation of parents in the promotion of the hygiene of the child, as is instanced by the Mothers' Congress, who for a number of years has attempted to awaken responsibility to the welfare of her children and to guide her in the study of child growth.

It is also a well-known fact that association and environment play a great part in the development of the child, and that it has been said that there is no criminal class, and that one way of preventing boys and girls from becoming criminals is to give them proper care and attention when young.

Recreation should not be only amusement: it should be educational as well, as the kindergartens. Keep the child busy.

On the hygiene of the teeth too much cannot be said, but it must not be forgotten that facial deformity and nasal stenosis may be prevented, according to Bogue, by operations on the temporary teeth of young children. Bony system largely developed through activity of muscles attached to bones, and therefore all operations to prevent small nasal passages, crooked nasal partitions, irregular teeth, high-arched roof of mouth, retreating chin and projecting chin, should be undertaken and, if possible, completed before the sixth year of life.

Proper mastication and proper breathing are brought about and mouth breathing eliminated.

Regarding the problem of feeble mindedness, it is claimed that 65 per cent. is hereditary. Regarding the other 35 per cent. there seems a contrariety of opinion whether sterilization is really the best means of prevention or the segregation of these unfortunates.

Mr. John A. Vogleson: I have listened with a great deal of interest and pleasure to the papers presented, and as I followed Dr. Ferrell's paper the thought running through my mind was concerning the two

distinct lines of endeavor in public health work: (1) Research work which is of high importance; and (2) work which more directly concerns the daily operations of the health department, namely, the practical application of knowledge already possessed which was so well expressed by Professor Fisher in his careful analysis and report in 1908 on "The Conservation of the National Vitality," when he said that the problem of prolonging life could be met to a great extent by the application of the knowledge already possessed by well-informed persons of the medical profession, to a reasonable degree in a reasonable way, and that is what we are trying to do in the Health Department of Philadelphia. It is superfluous, of course, for me to speak of the work of the Health Department when Dr. Neff has dwelt upon that; but there are one or two points in connection with the magnitude of our problem upon which I may say a word. In looking through our statistics the other day I was impressed with the fact that in 1892 over 30 per cent. of our total mortality occurred in children under two years of age, at which time the children under two years of age represented 3.5 per cent of our population. There was not much done in child hygiene activities as we recognize them today until 1910, when we had the beginning of our work in child hygiene in the Health Department as an organized line of endeavor. At that time the mortality for the year among children under two years of age was 25 per cent. of the total mortality, but they represented about 4 per cent. of the whole population. Passing through a shorter period to 1914, the mortality among the same group of children dropped to 20 per cent. of the total mortality and they still represent about 4 per cent. of the whole population. In the reductions of deaths among children we have one of our largest problems. The next group in point of magnitude with which we have to deal is, of course, the group affected with tuberculosis and diseases of the respiratory tract, and here we have next to the highest mortality, for from these causes about 20 per cent. of the total mortality occurs. That too is happily decreasing, but not as rapidly as is desired. Of the various lines of endeavor to which Dr. Neff referred I may add a word on the executive work of the Bureau. When I became connected with the Bureau of Health five years ago it seemed that our task was mainly to make people do a great many things they did not want to do. Happily that condition is changing and we are receiving more and more the coöperation of all classes of people and note an increasing interest in matters related to public health. One instance was that of the milk supply of the city. Formerly we had delegation after delegation coming to the department and protest after protest against measures necessary to provide clean milk. While the milk question is not entirely solved great progress has been made. Our Child

Hygiene division began in 1910 with a small and devoted band of nurses and its impress has been felt in every section of the city to which their work has been applied. The work at first was experimental and wards were selected for their highest infant mortality. Without exception every district to which a city nurse has been assigned has shown not only decreased infant mortality but a lowering of the general mortality as well. One of the greatest possibilities of advancing the work of the Department of Health for a more healthful city may be met by the addition of a sufficient number of nurses to adequately deal with the problem of infant welfare.

Dr. Seneca Egbert: I share with Dr. Abbott the optimism he has expressed regarding the work described by both Dr. Ferrell and Dr. Neff. We can divide the past twenty-five years into three periods: The first decade representing a period of almost inertia not only in the laity but in the medical profession regarding matters of public health. The next decade showed an awakening interest, and in the last five years the interest on the part of both laity and the medical profession has been remarkable. In anticipating the possibilities of the future, it is well that we occasionally take a backward glance of ten years and ask ourselves whether the results seen at the present could then have been thought possible. Dr. Abbott spoke of the economic importance of the conservation of life in regard to one disease, and I recall what Dr. Ferrell said about the carrying of the work into Egypt, Ceylon and the Philippines and his outline regarding malaria and hookworm disease. No man can predicate the economic results bound to occur in a short space of time. Just as General Gorgas has opened up a new world to the south of us by his work at Havana and Panama, so it seems that this work outlined by Dr. Ferrell is going to change the face of a large portion of the earth. We can all take a great deal of pride that so much of this work is in the hands of men of the American medical profession because we have known these men and because they are of us.

We have just as much reason to be optimistic in regard to infant mortality. The opportunity is great and the results obtained by Dr. Neff and by his successors in office, Dr. Harte and Dr. Ziegler, are remarkable in showing so great a reduction of mortality in such a short space of time. We must also give credit to the various branches of the Health Department, notably that in the medical inspection of schools under the direction of Dr. Cornell. There is other work also in the schools the benefit of which the youngsters carry home to parents. The parents make welcome the nurse who comes with the child who needs the care of a physician or nurse. Such work is educational and is marking the way for the next generation. Many people in this city do not yet realize what the

new water system has meant in the purification of the water of the city. Many believed that thirty millions of expenditure for our filter plant was extravagant. Comparatively few realize the return of over ten million annually in the saving of life and health and money capitalization to the city. This is true of every other department of work of the Health Bureau and some are beginning to recognize the value of the investment.

Dr. Ferrell: The paper of Dr. Neff presents in a forceful manner a number of the more fundamental problems involved in considering public health work. The infant welfare work he discusses so forcefully is of the utmost importance and should reach every home in the city, town and country. The need of larger appropriations is keenly felt in this as in every other branch of public health work. It unfortunately becomes necessary, therefore, for the health officer to consider measures that may be depended upon to secure the needed working capital for the health department. It is generally conceded that this is a matter of educating the people to appreciate the value of the work so that the task of the health officer must be devoted largely to educational work.

Some method must be followed in the educational work which will accomplish much at a small cost. In the field of agriculture it has been found that a concrete demonstration on a small scale has accomplished more than a similar investment could accomplish by any other method. For example, boys have been taught to grow a hundred bushels of corn on an acre of land where only twenty to thirty bushels were formerly raised by old farming methods. The lesson in growing corn teaches farmers of all ages in a way so convincing that the work of one boy who is willing to learn intensive methods from demonstrators frequently revolutionizes the farming methods in an entire community within a period of a year or two. The departments of agriculture where this work has been done has been growing by leaps and bounds and securing with reasonable effort the funds necessary to extend their work rapidly.

In public health work similar educational methods are practicable. A definite problem in the field of preventive medicine can be taken and a small circumscribed area in which to work can be selected. In the city it may be two blocks or a ward; in the rural sections it may be a school district or a township. With a limited force the cost for which is fixed, the work can begin by making a complete survey of conditions relating to the specific health problem under consideration. This will give a definite starting-point from which progress in the work can be measured. The work should be done as quickly as possible, and a second survey made. With a definite record of the time, cost, and results in hand it is possible to present the matter of the extension of the work to the people as a concrete business proposition. When this can be done on a basis

which will convince them that the voting of additional funds for the extension of the work will represent a paying investment the funds will be forthcoming. It is only on such a basis that industrial corporations can find additional capital for expansion. As health officers in the business of protecting health, saving life, increasing mental, physical and economic efficiency, we should be prepared to place our work on a sound economic business basis that will establish confidence with the people and win their enthusiastic coöperation. Once established on this basis the growth of the health departments in scope and in usefulness will be phenomenal.

MODERN MILITARY HYGIENE AND CAMP SANITATION[1]

By VICTOR C. VAUGHAN
ANN ARBOR, MICHIGAN

Four years of my childhood were spent in the midst of war, and I appreciate its horrors as few others can. I lived in a border state, and I was witness to the misdeeds and crimes of soldiers on both sides. I saw members of my own family hunted with the intention of shooting them down at sight. As a boy under ten years of age, it was not an infrequent occurrence to have a pistol placed in my face and to be asked where this man or that man was. Unlike George Washington, I could lie, and I did lie. I hope we shall have no more war, in this country at least. I do not believe in preparation for war, but I believe in preparation against war; not in preparation for offence, but in preparation for defence. I think that the world must be convinced by this time that the age of war has not yet passed, and that a nation which cannot fight is at the mercy of one which will.

My own little experience as a soldier did not amount to much. I went to the Spanish-American War for the same reason that I have done many things in my life, and that is because I have been unable under all circumstances to bridle my tongue. The Maine had been sunk; students in our University were excited; the President of the University came to me and said: "The students are all excited; they want to go to war. They have asked me to call a mass meeting, and I have consented. We will grant

[1] Read at a special meeting of the College of Physicians of Philadelphia, April 12, 1915.

them their request, and some of us older heads will talk to them and cool them down a little." I went to the mass meeting with a full intention of complying with the President's very reasonable request. There were many speakers, and fortunately or unfortunately I believe I was the thirteenth called upon that night. I suppose that I should be ashamed of what I said, but for some reason or other it has never troubled my conscience. I sat there and listened to speech after speech which drove me into a fury. One man admonished the students by saying: "Your first duty is to your college. If you leave, you will fall out of your class and may never complete your education." Another said: "Your first duty is to your father and mother, and you must consult with them before you enlist." Still another said, "Wait until all the unemployed are enlisted, and if there then be need you can enlist." After hearing speeches of this kind, I was called upon, and the first words I said were, "God pity the country whose tramps have to fight its battles. You do owe a duty to your father and mother, but your first duty is to your country. I would prefer to see the walls of these buildings crumble in dust than that you should refuse to serve your country in its time of need." The next day the Governor called me up by telephone and said, "I have read your speech. Your commission is on its way. You will report at Camp Alger within a week."

The first days in camp in Virginia we spent in vaccinating all, and I may say that, while we had a few sore arms as a result of this vaccination, there was, so far as I know, no case of smallpox in the army in 1898. With such a striking result as this, I cannot see how anyone can oppose vaccination for smallpox. In all human probability that disease would have added to our harrowing list of fatalities from disease had not vaccination been practised. We had scarcely finished the vaccinating when we had orders to proceed to Old Point Comfort and take ship for Cuba. My regiment embarked on the Auxiliary cruiser, Yale, which had formerly been, I believe, the City of Paris on a transatlantic line. There was no excitement on board until we were off San Salvador, when we hailed a vessel which neglected to promptly respond.

I was ordered to prepare the sick bay, which I did hurriedly, and then hastened back on deck just as we sent a shot across the bow of the strange vessel. With this salutation it "came to," and answered all questions in a civil and satisfactory manner. If my memory serves me right, it proved to be an English merchantman. Later we went around Cape Macey at night with all lights out, and, of course, not knowing what had happened since leaving Old Point Comfort, we were more or less excited. I went to bed rather late that night, and awoke next morning to find the sun shining brightly in my eyes. I felt with some chagrin that I had been a laggard, and rushed up on deck. Apparently we were directly under the Spanish flag, flying over Moro Castle. On the other side of our ship lay the American fleet, and it was a grand sight, grand enough to inspire the most lethargic. Our ship was ordered to return to Siboney and to disembark. We were carried ashore in lifeboats, inadequately manned, and many of us were dumped into the ocean and obliged to swin ashore. However, I fortunately succeeded in getting all my medical supplies onto land.

It is not my purpose to go into the history of that short campaign. Some sixteen hundred of our men were wounded, received their first dressings at the field hospitals, and were then transported, for the most part in army wagons, to the base hospital at Siboney. Here we had only thirteen medical men to take care of sixteen hundred wounded. At no time in my life have I laid any claim to being a surgeon, but in dressing these wounds a bacteriologist rather than a surgeon was mostly needed. We stood at the operating tables almost continually from Friday to the following Wednesday morning. All we had to do was to properly dress the wounds of entrance and of exit. In all the soldiers whose wounds I dressed, several hundred, I found only one lodged bullet. It was said that this man was lying on his side with one leg over the other when he was struck. Experts claimed that the bullet had fallen, at least, it made a keyhole wound through one thigh and practically through the other, lodging directly under the skin of the second thigh. I split the skin and took it out. It

is the only relic that I have of a bullet taken from a wounded man. I chose an expert barber to assist me at my table, and we proceeded to take care of the wounded men much as we dress rabbits in the laboratory in making physiological experiments. The region around the wound was thoroughly washed with an antiseptic. I preferred a 10 per cent. solution of lysol. This had served me so well in the laboratory that I preferred to use it in dressing the wounds. The barber was instructed to shave away from the wound, after which iodoform gauze was applied and held in place by adhesive strips. Each man dressed the wounds after his own fashion. We had only one cardinal rule and that was that no one should use a probe. On the whole the results were exceedingly satisfactory. There was relatively but little infection. Personally I took care of many wounds transfixing the chest. Some of these men coughed up blood for a few days, but there were no serious results. There were a few real surgeons with us and wounds of the abdomen were turned over to them.

On the very day that we finished the first dressings of all, yellow fever made its appearance. Your former townsman, Dr. Guiteras, was with us as an expert in the recognition and treatment of this disease. Recognizing the fact that serious trouble might follow if the wounded became infected with yellow fever, all who could be transported were placed on board ships and returned immediately to this country. The wisdom of this procedure was shown by the results. No wounded man died of yellow fever and, so far as I know, no wounded man sent directly north was seriously ill of this disease. I had just finished my work at the operating table on Wednesday morning and had sought my hammock expecting to have a sleep, when I met some men with a sick man on a stretcher. The bearers said that the man had been brought down from the trenches some miles distant, and that he was very ill and needed attention, but he was at that time sound asleep. I asked them to place the stretcher under my hammock, and the man slept and so did I. Finally I was awakened by the man vomiting. The black vomit was evidence enough, so I called for Dr. Guiteras and said that we had a case of yellow fever.

He and I took a hand-car and went up on the mountainside some distance above the sea, and located a yellow fever camp. Within a few days we had many hundreds of cases. We were but poorly supplied with facilities for diagnosis, and we tried to divide the cases into those with malaria, those with typhoid fever, and those with yellow fever. I suppose that we made some mistakes, but fortunately not many. Having no microscope, we could not look for the plasmodium of malaria. We had to rely largely upon an imperfect history and the condition of the patient in order to determine which one of the three diseases he had. We sent to the yellow fever hospital every man who had albumin in his urine, and it is rather remarkable that we did not make many mistakes. None of a serious nature, so far as I know, were made. About a week after the appearance of the first case of yellow fever, I came down with the disease myself. I happened to be at the surgical hospital that day, and had been busy in the hot sun in charge of several hundred men who were cleaning the camp. A severe pain in my back made me realize, or at least suspect, that I had been bitten by an infected mosquito. Inasmuch as the wounded had been sent home, there were large tents, each with many cots vacant at the time. I went into one of these tents and occupied a cot. Then I sent for my old friend, Guiteras. He looked me over and said, "Just a little malaria." I think that Dr. Guiteras came to my bed half a dozen or more times that night. I pretended to be asleep, but through my partially closed lids I could see the anxiety in his face. Early the next morning, he came whistling and with an air of one who has slept well, and said, "Don't you think it is a great deal better at the yellow fever camp?" I agreed that it was, and he took me there.

It may be of interest to know that most of the cases of yellow fever were typical. In many the temperature ran to 106° where it continued for four or five days and then disappeared by crisis. I know that in my own case the temperature fell from somewhere above 105° to normal within a few hours. Fortunately the yellow fever was, on the whole, of rather mild type, the deaths being 13 per cent. After partial recovery from yellow fever, I was

placed in charge of a hospital ship and ordered to proceed to Tampa. In Tampa Bay the Florida authorities stopped us and would not permit us to land. We were detained here several days. In the meantime, some four or five other ships, loaded with sick, arrived at the same place. I had telegraphic instructions from the Secretary of War to pick out the best of the ships, put all on board, and proceed to New York. This I proceeded to do, and we reached New York harbor on the night that peace was proclaimed.

I may say here that strange as it may seem, we had more or less diphtheria from the time of leaving Old Point Comfort until we reached New York. Unfortunately no one had foreseen this, and we had no antitoxin. The only death on my ship on the return was from diphtheria, and this occurred between Tampa Bay and New York.

After my return, General Sternberg appointed a commission to investigate the fever then prevalent in the camps in the United States. This Commission consisted of Major Walter Reed, afterward one of the discoverers of the transmission of yellow fever, Dr. Edward Shakespeare of your city, and myself. It is concerning this investigation that I wish to speak especially to you tonight. The Spanish-American War did not amount to much in a military way, but from it came some things of special interest to the medical profession and to the general public.

In the War of the Rebellion, there was considerable discussion concerning the nature of the fever then so widely prevalent among the Northern soldiers. As early as 1861 a Medical Board was appointed to investigate this matter. However, nothing definite came out of this, and in 1862 another Board was appointed with special reference to reporting the diseases. Major Woodward of the second Board believed that the fever then prevalent in the army was due to coincident typhoid and malarial infection, that is, that the patient had both infections, and at his suggestion the term "typho-malaria" was adopted in 1862. This term was used throughout the Civil War, and there were fifty-five thousand cases reported under this diagnosis, with about 10 per cent. of

deaths. The profession of this country adopted Woodward's name of "typho-malaria" fever, but never accepted his idea of the disease. The profession and the laity believed "typho-malaria" to be a severe form of malaria, and not due, even in part, to typhoid fever. Many of the profession welcomed this escape from the necessity of making a diagnosis of typhoid fever. "Typho-malaria" came to mean severe malaria but less virulent than typhoid fever. This was not Woodward's idea at all. As stated above, he believed that the two infections existed simultaneously in the same individual. The term "typho-malaria" was used more or less in this country with the general meaning attached to it up to the time of the Spanish-American War.

When troops were called for on the proclamation of war against Spain, in round numbers one hundred thousand men enlisted. Nearly every State furnished its quota. Regiments were hastily assembled, inadequately drilled, often inefficiently officered and rushed into camps with the result that within six weeks fever was prevalent in every camp in the United States. There were all kinds of theories proposed to account for this fever. Some said that it was due to change of climate, Northern men being transported quickly and in masses to the South; others said that it was due to bringing so many men together in the same camp. However, when our Board came to study the matter, we found that no regiment suffered more severely than a Minnesota regiment encamped on the fair grounds at St. Paul. Two or three regiments encamped in New York also furnished long lists of cases. Evidently, then, the fever was not due either to change in climate or to the concentration of many regiments at the same point. One of the oldest theories concerning infectious disease is that it is due to miasma or effluvium from the earth. I believe that this theory was first proposed by Hippocrates, who reasoned that if many people are sick at the same time and place, the illness must be due to that with which all come in contact, and what could this be but the air. It is difficult even for medical men to get away from this idea that disease is due to miasma and it is a theory which still plays a large part among non-medical

people. Thoroughly educated men at Chicamauga said with baited breath "The word Chicamauga means River of Death," and that the disease was not typhoid or malaria but Chicamauga fever. However the fever did not disappear when one corps was assembled on the healthful hillsides of Camp Meade in Lancaster County, Pennsylvania. It will be seen that it was of the greatest importance that the nature of this fever, its transmission, and everything pertaining to it should be studied most earnestly.

Our Board proceeded at once to Camp Alger in Virginia. Here we saw hundreds of cases which in our opinion were typhoid fever, but which in the opinion of many others among those attending the cases, were malaria. The question had to be settled positively in some way. Therefore we asked the Surgeon-General to allow us to find men who could make the agglutination test for typhoid fever and who would recognize the plasmodium of malaria, and properly equip these men and place them in every camp in the United States. I wish to emphasize the fact that this work could never have been done had not the agglutination test been thoroughly worked out beforehand. In other words, the animal experimentation which began with the work of Charin and Rogers in 1888, advanced by Metschnikoff, developed by Gruber and Durham, and brought to fruition by Widal, was necessary in order for the Typhoid Commission to settle this question. It is probable that in all the work done on the agglutination test hundreds and possibly thousands of animals have died, but this work enabled the Commission to reach definite conclusions, which have resulted in the saving of twenty thousand lives a year in this country alone from one disease, typhoid fever.

At Jacksonville, Florida, most of the army surgeons believed that the fever was malaria. We asked the commander of the corps to order his surgeons to pick out fifty cases of what they thought were typical malaria and that these cases be turned over to the Commission for examination. These fifty patients were examined by Dr. Craig, and every one of them found to have typhoid fever. Inasmuch as some of the medical men were not satisfied with this, one hundred and fifty more cases were selected

and examination showed that they were all cases of typhoid fever. It may be interesting to remark in this connection that among something like twenty thousand cases of typhoid fever found in the camps in 1898, there were less than twenty cases of coincident infection with typhoid fever and malaria. Moreover, in the cases of coincident infection, it was found that the symptoms of malaria were held in abeyance during the attack of typhoid. There is therefore no such disease as "typho-malaria" either in the sense used by Woodward or that understood by the profession in general.

Having ascertained beyond any doubt through the aid of the agglutination test and the search for the plasmodium of malaria that the prevalent fever was typhoid, the question as to how it arose and how it spread became of the greatest importance. The members of the Commission began this investigation believing that typhoid fever is almost exclusively a water-borne disease, and we expected to find infected water in every camp. At Camp Alger the water was taken from driven wells, some of them over a hundred feet deep, and the most careful examination of these waters failed to show the slightest evidence of infection. At Jacksonville, Florida, the evidence against the disease being water-borne was absolutely conclusive. On one side of the water supply was the city of Jacksonville with about thirty thousand inhabitants; on the other side were the camps with about thirty thousand soldiers. Civilians and soldiers were drinking the same water. Among the inhabitants of the city there were seven cases of typhoid fever; among the soldiers there were nearly seven thousand cases. Evidently it could not be the water unless the water became greatly polluted after it reached the camps. Like evidence was furnished at other camps so that we were compelled to abandon the theory that typhoid fever is exclusively a water-borne disease.

Further investigation showed most conclusively that at least 60 per cent. of the cases of typhoid fever in the American army in 1898 was due to contact infection, and that about 15 per cent. of the cases were transmitted by the agency of flies. It was not at all difficult to prove the latter. We noticed in our earliest inspections that typhoid cases were rare among men who ate

their meals in screened mess tents. Later we sprinkled lime over the uncovered filth in latrines and saw later on flies with their feet whitened with lime walking over the food which the soldiers were eating. It did not take long to convict the fly. However, the greatest work done by this Commission was to prove that typhoid fever is in the great majority of instances due to contact. I wish at this point to state that the detail of this investigation was largely worked out by your former colleague, Dr. Edward Shakespeare. He spent day after day, week after week, and month after month in tracing soldier after soldier from his home into his company, at his tent, placing him among his colleagues and proving finally that tentage, blankets, bedding, clothing, and person became infected and served in the transmission of the disease. This great work done, as I say, so largely by Dr. Shakespeare, has been confirmed since that time in practically every part of the world. Drigalski, nine years later, stated that 64 per cent. of the cases of typhoid fever in Germany are due to contact. It is worthy of note here in passing that Drigalski makes no mention of Shakespeare's work done nine years before his.

Now, what does all this mean, and how far are we today interested in it? What fruit has it brought us? In 1898 about thirty-five thousand persons died each year in this country from typhoid. Now, with a greater population, not more than twenty thousand people die. This means that about fifteen thousand people are being saved each year from death from one disease, and this saving was secured, and could have been secured in no other way than through animal experimentation. Again, the investigations of the Typhoid Commission showed that typhoid fever in armies and in camps of all kinds is due to pollution, pollution of the soil, pollution of the clothing, blankets, tentage and persons. It is probable that hundreds and possibly thousands of guinea-pigs and rabbits have been killed in order that fifteen thousand people might be saved every year in this country alone from death from typhoid fever.

I have stated that we had malignant diphtheria on the Cuban

campaign and that we did not have antitoxin. Much illness and some deaths would have been prevented had we been supplied with this wonderful curative agent. This also is an illustration of the great value that animal experimentation has been to humanity.

In 1880, the first year in which a reliable census of the United States was taken, out of every one hundred thousand people three hundred and twenty-six died every year of tuberculosis. In 1912 the deaths from tuberculosis in this country had been reduced more than 50 per cent. How many guinea-pigs were sacrificed in order to bring about this saving in human life? Was it worth it? Has man benefited by it? Has disease been lessened and death diminished? If the death-rate for tuberculosis in this country in 1901 had continued during the following ten years, there would have been two hundred thousand more deaths from this disease alone than did occur. The average of life in the United States has been increased four years in the last ten years and ten years in the last twenty-five years, and this has been done largely by knowledge obtained through scientific animal experimentation.

I will mention another thing of importance which has resulted from the study of typhoid fever in 1898. The Commission went into the investigation believing that sickly men and men of less robust health would be more likely to acquire typhoid fever and to die of it than strong, robust men. The records of the regular army furnished splendid opportunity for a study of this kind. There were men who had been serving for many years, and of these we had a complete medical record. Of some six or eight thousand men who might be called sickly or not up to par, about 6 per cent. had typhoid, while out of more than forty thousand men who were robust and who had never been on "sick report," 16 per cent. had typhoid fever. When we come to think about it, this is easy of explanation. When unusual duty is to be performed the strong man goes, and men of this class are the ones most frequently exposed to infection. Typhoid fever is more prevalent among healthy young adults, and especially among healthy young male adults because of their greater and wider range of

activity and more frequent exposure. Men have typhoid fever more frequently than women; adults more frequently than children; the young adult more frequently than the old, for the same reason. However, another thing was ascertained which may not seem so reasonable. The mortality among the robust is greater than it is among the weak. This is not new. More than one hundred years ago it was observed that typhus fever kills the strong and vigorous rather than the weak. When a strong, vigorous man is attacked with typhoid or typhus fever, his body cells put up a big fight, and they destroy the bacteria so rapidly, setting free the bacterial poison so abundantly, that the individual dies. There have been those who have held that the infectious diseases in the long run benefited the race by killing off the weak. Even Herbert Spencer fell into this error. Infectious disease, like war, kills off the most fit, the robust, and the vigorous. This was noticed in the great epidemics of the plague in the Middle Ages. All these things we have learned by animal experimentation, or we have learned to profit in our prevention and treatment of these diseases by animal experimentation. In the Civil War we learned nothing from our experience with "camp" fever. We would have been in a nearly helpless position in trying to solve the problem in the Spanish-American War had it not been for animal experimentation. The English did not learn a thing from our experience in the Spanish-American War, and they paid dearly for it in the Boer War. We must not think that our experience in the Civil War was unique. In the German invasion of France in 1870 every regiment was infected with typhoid fever, and their experience was the same as ours in the Civil War. It was impossible in 1898, so widely prevalent was typhoid fever in this country at that time, to bring together a thousand men of military age without having in their midst an average of four already infected. With the camp insanitation of that time the disease rapidly spread.

The first war in which typhoid fever was a neglible quantity was the Russo-Japanese War. It was true practically on both sides. One of the medical men of the Japanese army said to me:

"What we know about typhoid fever we learned from the United States and from Europe, and we put it into practice and profited by it."

The whole science of preventive medicine lies on the foundation of animal experimentation. Until men began to experiment there could be nothing more than a germ theory of disease. Now that bacteria do cause disease has been demonstrated just as thoroughly as that two and two make four. Disease has been lessened, life has been prolonged, and the general well-being of the people has been improved. With such a record as this, I am sure that no one can question the value of animal experimentation.

CARDIOVASCULAR POISONS: THEIR METHODS AND RESULTS[1]

By ROBERT N. WILLSON, M.D.

To those who know the heart simply as a muscular pump, the function of which is to supply the various parts of the body with blood, the term cardiovascular poison will mean little more than a drug which causes the heart to misbehave or to functionate badly. Generally speaking, the heart is a much neglected study. The why and the wherefore of its phenomena, its minute anatomy and physiology, their relation to clinical and physical signs, and their influence upon and response to the action of drugs and other toxins, all form phases and spheres of heart study, a thorough grasp upon which is as essential to intelligent bedside observation as it is to laboratory investigation.

It is well to realize that we know only two and perhaps only one true cardiac tonic, oxygen, and perhaps certain forms of sugar. Again, it will be of advantage to forget altogether the old belief that the heart is lacking in nervous tissue. We are often reminded "that there are few nerve elements in the heart, and none to be found in the atrioventricular bundle," or in the other foci of cardiac nodal tissue. And yet it is no very recent discovery that if any human organ is over-rich in its nervous supply, the heart is that one. It is an exceedingly important and also a not recently acquired item of knowledge that, probably, with a view to the maintenance of intracardiac pressure, one of the main nervous distributions in the heart is subendocardial. The sinus node contains a veritable network of vagal filaments;

[1] Read May 5, 1915.

and the specilized nodal tissue itself is composed of cells and fibers which merge now into nervous structures and now into muscular. These are features of all nodal tissue, including that recently discovered in the intestinal wall by Arthur Keith, which seems to differ neither in structure nor function from the specialized tissue of the heart.

Up to the present moment we have failed to solve the functional riddle of the myriads of sympathetic ganglia in the heart. The mere knowledge of the existence of these structures is, of itself, important, even though for the immediate present we appear to have been blocked in our attempt to discover their exact method of working. Especially in relation to the administration of medicaments is it essential to realize that the heart is not simply a nerveless muscle. Even more helpful is an appreciation of the fact that notwithstanding all the accepted conclusions on the subject, it seems more and more probable that the cardiac nervous structures enter in greater or less degree into the inception and the discharge of each and all of the main functions of the heart.

With this simple introduction, I wish to discuss briefly three groups of cardiovascular poisons, meaning by the term substances manufactured within or introduced into the body which injure and destroy instead of nourishing the various cardiac tissues. I have chosen the term cardiovascular advisedly in the realization that clinically and practically those substances which stimulate and strengthen and nourish the heart, exert a similar influence upon the very similar tissues in its extension, as it were, the arterial tree. Just so the substances which poison the tissues and deplete the forces of the heart tend to injure and to render incompetent the bloodvessels. This does not mean, however, that the pharmacological action of every drug would be primarily and secondarily identical upon the two unless essentially poisonous for both.

The first of the groups of cardiovascular poisons is perhaps most often in evidence, though by no means always credited with the mischief for which it is responsible. I refer to the

I. Decomposition Food Products. These are at work from childhood to old age. They constitute, I believe, the underlying and causal factor in the production of the arterial changes and the hypertension which contribute so actively to the cardiac disease of later years. In babyhood the main influence in their production is usually an oversupply, less often an unclean or improper form of food. This factor of gross overfeeding, and consequent gastro-intestinal decomposition, is operative, as a rule, throughout childhood, and well past puberty. Occasionally it is continued through life. It exerts two influences upon the heart, one toxic, the other mechanical. Beginning with the child's admission to the general diet of the family table enters still more forcefully the factor of indigestible food, not infrequently taken in unreasonable excess. We all eat too much, for our individual needs; we all indulge in many things better calculated to disturb than to further nutrition; and most of us send them on their way toward the stomach and the bowel very imperfectly prepared for assimilation. As a direct result, whether babies or adult working units, or old men and women, we have at all times within us digestive tubes much more foul than they should be, from which we absorb the poisonous end-products of not only an excess, and of improper patulum, but also of the altogether suitable foods. The popular present-day name for this condition is intestinal stasis, and the surgeons are manifesting a cordial interest in Jackson's membranes, Lane's kinks, and similar obstructions as its cause. Our grandparents knew better, and though they stuffed the grandchildren from the breast to puberty, "too much food" was their lay diagnosis and castor oil their very rational and effective cure. I think it fair to assume that a timely and intelligent and persistent use of the same regimen would relieve by prevention, if not cure, very many of the conditions diagnosed as Lane's kinks today.

Intestinal decomposition implies at once the manufacture and the absorption of toxic material, in part strictly chemical, in part purely bacterial, in part consisting of normal food and products, poisonous perhaps to a given individual, though utiliz-

able by the majority of human beings. These toxic substances act in one or all of three ways: (1) through a chemical toxemia and a direct poisoning of the body tissues; (2) through a bacteriemia, as in the frequent colon bacillus infections, and (3) by the formation of poisonous gases which not only are in some measure absorbed, but, by mechanically displacing and discommoding, embarrass organs above and below the diaphragm through gastro-intestional distention. In all three of these forms of food poisoning the first recognizable effect is upon the cardiovascular system. I have experimented upon laboratory animals and upon myself, and have questioned very carefully patients in my care with a view to gaining light upon this point. From all three sources I obtain ample evidence that the heart and the vasomotor system experience very early the influences of a food toxemia of whatever nature. Usually there is a marked quickening of the cardiac action, often distinct palpitation, almost always in the acute stages (before collapse) there is a marked elevation of both the systolic and diastolic pressures. Later, as the heart begins to tire, the systolic pressure may fall and the rhythm become irregular. Not infrequently I have seen distinct signs of cardiac dilatation in the entire absence of abdominal distention, *i. e.*, not a mechanical embarrassment. I have just finished a nine-months' study of a giant tom cat in which were noted on a single meal per diem a normal pulse rate of about 100, a single formed stool, and an apparently well, lazy, affectionate cat. On two daily meals (one of milk, one of mixed food from the table) the cat ran a distinctly angry cardiac action and rate of about 120, its stools numbered two and three and were exceedingly offensive, and the cat was evidently irritable and ugly when disturbed. On three meals daily, two of them containing a small quantity of meat, the stools became numerous, diarrheic in character, occasional blood streaking could be noted, the animal manifestly suffering from an intestinal inflammation secondary to the decomposition of food in excess. The cardiac action averaged 120 to 130, the apical impulse was no longer bounding and angry and of high tension, it was rather diffuse and weak,

and an occasional irregularity could be detected. The heart and the vessels were incompetent as the result of a toxemia.

This series of experiments was carried out repeatedly on various kinds of food, with identical results in all instances. The excess of animal proteins would poison the animal more promptly than a strictly vegetable dietary, but the main factor was manifestly the excess of supply, and not the kind furnished.

Long before it had occurred to me to test out in a laboratory animal the theory of cardiovascular poisoning through decomposition food products, I had suspected the relation of cause and effect owing to numerous personal experiences. For years I have been in the habit of taking either no third meal in the day, or else a simple saucerful of boiled rice with milk and sugar. I found that the moment this boundary was overstepped I began to receive signals from my cardiovascular system that were finally too definite to be ignored. Within an hour after a moderate evening (third) meal my whole body (not the abdomen) began to feel full and tense. The hands and feet, the thorax, the head, especially the skin surfaces, felt full and tense and hot. The pulse rate in a short time increased from 20 to 40 beats per minute. The systolic pressure (Stanton apparatus) has on more than one such occasion risen to 160 and 170 (my normal is 130), and the diastolic to 110 and 120. After retiring I could feel my cardiac action from head to foot to a most uncomfortable degree. It seemed as though the bed responded to the cardiac impulse, so general was the hypertension and overaction. Always following such an experience there would occur during the night hours, or during the next morning, several dark offensive, often liquid stools. Only upon their evacuation would the toxemia and excessive cardiovascular tension disappear and I become comfortable. I have questioned many intelligent and observant physicians and laymen, and find that my experience is not an isolated one by any means. As with the cat, the idiosyncracy, is not one of particular classes of foodstuffs. It is usually one of quantity and excess, though I learned long ago that a number of the fruits and vege-

tables which Mendel[1] and other laboratory authorities believe are fully assimilated as basal and alkaline products are toxic for me and, as regularly as I venture to use them just so surely they produce in me an acid toxemia within an hour or two of their ingestion.

In connection with an actual infection of the blood stream and consequent harmful effects upon the heart and vessels, I have been interested for a considerable number of years in the presence of myriads of bacilli of the colon group in the non-decomposed urine of persons experiencing gastro-intestinal disorders. Only recently have I begun watching for and noting the frequent implication of the cardiovascular system in such individuals. Not always in these colon infections was there hypertension and overaction of the heart present. Occasionally there was a systolic blood-pressure of 100 or lower, and a diastolic pressure of 55 or 60. I recall two physicians each weighing nearly 200 pounds, in whom the systolic pressure averaged 100, and the diastolic 75, Rosenow's recently published cultural experiments[2] may throw some light upon these clinical findings. Of his 20 (14 acutely) diseased appendices removed by operation he found in 6 pure cultures of the colon bacillus in the pus within the lumen, and in predominating excess, though in company with streptococci or other bacteria in the remainder. As the appendix reflects in a considerable measure the conditions of the entire bowel, it seems fair to assume that somewhat similar bacterial findings will prevail in disorders of the main digestive tube. If correct in this assumption, we need not seek far for the explanation of the toxic effects upon the heart and vessels in the many forms of food poisoning which seem possible of understanding only upon a microörganismal basis. I refer to such phenomena as the toxic and overdriven heart and vascular hypertension in association with a bronchitis (evidently toxic), and widely separated joint and muscle pains, and skin eruptions other than those typically vasomotor—all temporary, but appearing shortly after a dietary

[1] Jour. Amer. Med. Assn., September 5, 1914.
[2] Jour. of Infect. Dis., March, 1915.

indiscretion, and subsiding only after a thorough cleansing and approximate sterilization of the gastro-intestinal tract.

Still another series of cases will base its cardiovascular symptomatology upon the presence of gases in the intestinal canal. Their influence is apparently due to their absorption as such and to a direct toxic action upon the cardiovascular as well as upon all the body tissues. I can easily believe after observing a number of such instances that the distress in typhoid tympanites is not altogether mechanical, and that it is not entirely due to overdistention and to dislocation of the heart from its normal position. The intestinal gases appear toxic and I have no doubt the patient absorbs them with the same effect upon the blood and cardiovascular system as though he were to inhale illuminating or some other noxious gas. Undoubtedly the mechanical factor is always in evidence in the form of a transverse position of the heart and an interference with its intake and output of blood. But probably the toxic influence is the more prompt and serious. It is remarkable how completely incapacitated an individual may be, who has ineffectually emptied his rectum and possibly the sigmoid, whereas higher up in the large bowel or in the coils of the small intestine some particle of food is undergoing decomposition, and meanwhile is filling not only the intestine but the blood and lymph circulations with poisonous gases. These may be retained in the bowel for hours, especially at night, slowly filtering into the blood. Meanwhile the patient suffers all the symptoms of a toxemia and of mechanical discomfort combined. The diastolic pressure is usually elevated, also the systolic if the heart muscle is still intact. The vessels pulsate and throb, the skin is pale, the head aches, the tongue is coated, the breath foul, vertigo is often distressing, not infrequently the hands and feet feel distended and swollen. Finally a thorough housecleaning of the gastro-intestinal tract causes the expulsion of the offending food substance and ahead of it an unconscionable quantity of gas. Whereupon the blood-pressures resume their normal level, the heart returns to an orderly method of procedure, and slowly the nausea, pallor, headache, and the puffiness of the

hands and feet subside. It has been necessary to refer to the various toxic symptoms other than those of the heart and vessels. I have done so briefly, however, as it is my object to direct attention to the primary influence of the food toxemias upon the cardiovascular circulation. Wherever the arterial and capillary ramifications penetrate, there will be found indications of a toxin or toxins at work. Dale,[1] and later Eustis,[2] have attributed the main and usual effects upon the blood-pressure to certain of the amino acids, notably the derivatives from leucin and tyrosin. Eustis, by removing the proteins in large measure from the dietary has in many of his patients caused a distinct lowering of the blood-pressure with the disappearance of the general symptoms of toxemia. Other amines have been found working similar cardiovascular mischief, as oxyphenylethylamin in overripe German and American cheeses by Winterstein and Küng,[3] and by Van Slyke and Hart.[4]

I have already mentioned my personal experience with certain non-protein foods, among them the highly acid vegetables such as tomatoes and rhubarb, also such fruits as the apple, orange, lemon, peach and strawberry, and the cantaloupe as perhaps the worst offender of all in producing an identical picture with that which follows either a protein excess or an overindulgence in any kind of food. Shellfish, unless used in the strictest moderation, will also produce toxic effects. It would seem, therefore, as though the clinical symptoms suggesting a toxemia, especially as reflected in the cardiovascular system, are to be ascribed in the main to poisons elaborated in the intestine, to be sure, but not from any one group of foodstuffs. The only requisite would seem to be that a given food substance or one of its constituents or end-products shall prove toxic for its individual host. Furnish the summer heat of the bowel, retention for hours, and the decomposition of masses of undigested and often indigestible food, the presence even of food substances innocuous and tissue-

[1] Jour. of Physiol., March 22, 1909, xxxviii, No. 4.
[2] Southern Med. Jour., May, 1912, pp. 442–447.
[3] Mittheil. Zeitsch. f. physiol. Chem., 1909, lix, 138.
[4] Bull. 231, New York Agricultural Experimental Station, 1903.

builders in other individuals, only provided they are toxic for the given one—here we have all the conditions favorable to the production of acute cardiovascular crises, which, if repeated often enough and persistently enough will result in cardiovascular disease. I believe most thoroughly as the outcome of many experiences such as I have described in myself and others, that when we begin to look to the gastro-intestinal tube and its misuse for the origin and cause of hypertension, arteriosclerosis, the myocardial degenerations, now and again hypotension, just so soon will we comprehend the fundamental factors inducing the all too prevalent premature old age. Its other name is preventable cardiovascular disease.

II. Microörganismal Influences. A second class of cardiovascular poisons makes its attack from without. No less insidious, not a whit less difficult to avoid, the infectious diseases, including tuberculosis and syphilis, approach without adequate warning, and the harm is accomplished before the danger is realized. I shall consider four of these diseases as furnishing examples of the methods employed by the different members of the entire group. Syphilis, tuberculosis, rheumatism (so-called), and diphtheria, illustrate fairly well the various forms of micro-organismal invasion of the heart and vessels.

Syphilis and *tuberculosis* begin with heredity: Very frequently do we find the children of luetic or tuberculous parentage the subjects of myocardial or valvular defects or lesions. In the case of syphilis the conviction is growing that in some unexplained manner the disease favors developmental defects. T. R. Whipham[1] has recently reported two instances of congenital heart block, probably in both cases due to a congenital septal defect. Especially is this syphilitic relationship true of vascular lesions. I have a number of times seen newborn babes with arteries that would have done credit to the latter end of life, rather than its beginning. I have in my collection a specimen from a little child of four years, showing a ruptured thoracic aneurysm and extensive disease of all the cardiac valves. The brachial

[1] Proc. Roy. Soc. of Med., Lancet, 1915.

and radial and temporal arteries resembled those of an old man. Valvular syphilitic disease ranks next in frequency, if it does not actually surpass, the incidence of lesions due to the acute rheumatic infections. Warthin[1] has well described the myocardial lesions of syphilis, some or all of which are to be noted in the heart of every syphilitic. Gummata, while not rare, are comparatively infrequent findings. Vaquez,[2] Keith and Miller,[3] and Harbitz[4] have all reported instances, and I myself have seen several. Brooks[5] found a true cardiac gumma present in 5 out of 44 syphilitic cases examined. Colonies of spirochetes are almost invariably present, often indicating the areas of degenerative change. The usual lesions consist of fatty degeneration with marked atrophy of the cells and fibers, or of simple atrophy as the result of the presence of the spirochetes. Myxomatous areas are found freely in the hearts of congenitally syphilitic infants. Interstitial changes are present in all syphilitic hearts, varying from a simple edema to a profuse fibroid proliferation, with new capillaries and always with perivascular colonies of spirochetes. It would seem that the heart shows an almost invariable involvement in syphilis. In view of the lack of tendency to effective repair of myocardial lesions it would also seem as though we had in the implication of this vital organ one of the strongest indications for the thorough-going eradication of the spirochetes from the entire economy.

The *tubercle bacillus and its toxin* also furnish us with an invariably diseased heart. We have not far to seek for the reason when we remember that Besanti and Panisset have demonstrated the presence of tubercle bacilli in the heart's blood four and five hours after being administered in the food. Nothing is more typical than the small heart of tuberculosis, driven far beyond its normal rate, in an almost characteristic, irritable toxic overaction. The early and constantly low systolic blood-pressure of the tuberculosis patient indicates the severity of the toxic

[1] Amer. Jour. Med. Sci., March, 1911, p. 398; May, 1914, p. 667.
[2] Presse Méd., 1907, xv, No. 8.
[3] Lancet, November 24, 1906.
[4] Magazin. f. Laegevdensk., November, 1914, lxxv, No. 11.
[5] Amer. Jour. Med. Sci., October, 1913, p. 513.

action upon the cardiac muscle and nervous structures. Not all cases show the small heart, and not all present a lowered blood-pressure, but a sufficient number do to make both distinctive features of the physical picture. In most instances of long-standing tuberculosis the walls of the vessels are thickened and more or less inelastic, and offer a mechanical obstacle to the output from the heart, thus draining still further upon its resources. Myocardial wasting goes hand-in-hand with that of the general musculature of the body. At first there is probably a moderate hypertrophy of the wall of the right ventricle to compensate for the disturbance in the pulmonary circulation. In the majority of advanced cases of tuberculosis the lungs and pleura pull the attached pericardium, and with it the heart, out of the normal positions and relations. Soon the toxins, always of a mixed infection, malnutrition, exhaustion from overwork, and an increasing poverty of normal blood, lead to definite myocardial degenerative changes. These are, as a rule, not tuberculous in character. They include all the gradations of fibrous and fatty change, the result of long-continued exhaustion of muscle, ganglion, and nerve. Rarely miliary tubercles are found in the myocardium, and even in the walls of the vessels. They seldom or never give clinical evidence of their presence. The endocardium is occasionally attacked by the tubercle bacillus or by the organisms underlying the customary secondary infection. Also the pericardium is not infrequently implicated, more often in the child than in the adult.

I have cited tuberculosis and described its cardiac lesions as illustrating a typical toxemia, and an overtaxed, often underdeveloped, cardiovascular mechanism. And yet we must be prepared at any time to hear that as with the spirochete, the tubercle bacillus is present everywhere throughout the cardiac musculature. I have found it in the heart blood of a tuberculous guinea-pig, and have no doubt, especially in the early stages of the bacteriemia, it makes its way into every capillary supplying every cardiac muscle fiber.

The *acute rheumatic infections* form, at the present moment, a

difficult subject for discussion. That which is certain today may be disproved literally tomorrow. We are in an uncertain, and a transition stage with respect even to the etiology. As a clinical picture rheumatism means something very definite. As a micro-organismal invasion it has already been conceived to mean many different things. Recent studies render it likely that the majority of instances are due to some one of the various strains of streptococcus. It seems probable, however, that the symptom-complex may occasionally be caused by the invasion of the blood stream by any one of a number of microörganisms, including the staphylococcus, pneumococcus, and possibly the influenza bacillus. Rosenow's demonstration of the intertransmutability of the pneumococcus and the streptococcus, with the Streptococcus viridans as the intermediate stage, has opened a new phase of bacterial life which bids fair to modify our ideas concerning certain of the specific infections.

In both children and adults the cardiac involvement in the rheumatic infections is a carditis. All of the structures are involved, especially the myocardium. Even the pericardium shows a frequent tendency to implication. The disturbances frequently noted in the cardinal functions of the rheumatic heart, such as auricular fibrillation and flutter, gallop rhythm, pulsus alternans, and cardiac asthma, all point to grave and usually permanent structural change. Whatever the causal organism or organisms the disease is a bacteriemia and the heart manifestly suffers from the presence of the microörganism as well as from the toxemia. It has been the general impression that the valves bear the main brunt of the storm. This is by no means true. They suffer often enough, but it is safe to say that the myocardial lesions are of more serious import, whereas they are usually ignored. All grades of inflammatory involvement may be found in the muscle cells and fibers, from cloudy swelling to an interstitial edema or a fibrosis. Fatty degeneration and fibroid replacement are the two most frequent terminal processes, and upon and because of one of these processes is in due time usually superimposed the clinical picture of cardiac dilatation with rup-

ture of compensation. Another very characteristic lesion of the rheumatic heart infections is the so-called nodule of Aschoff, consisting of a focus of large (giant) cells, often multinuclear, and apparently fibroblastic in character. They are found in most, if not all, cases of true rheumatism. Fraenkel noted them in 17 out of 20 cases.[1] Thallheimer and Rothschild[2] found them present in 3 cases of chorea without arthritis. They were absent in 14 cases of endocarditis due to Streptococcus mitis, and also in endocarditic infections due to the gonococcus, staphylococcus, streptococcus, and pneumococcus.

In *diphtheria* we experience nearly 100 per cent. of instances of myocardial involvement, some clinically almost insignificant, others resulting in sudden cardiac death. In from 15 to 20 per cent. of all cases of diphtheria there are clinical symptoms indicative of the heart implication. Beginning as an acute myocarditis due to the bacteriemia as well as to the well-recognized toxemia, the changes in the cardiac muscle are found varying from a cloudy swelling to a wide-spread fatty degeneration. There is an increase in the size and number of the nuclei of the muscular fibers, with a decided tendency to destruction of the nucleus or even of the fiber itself. Fatty and granular degenerations account for most of the destructive change. Vincent found in one case of sudden fatality no recognizable change except loss of the striæ, and an increase of the connective tissue around the bloodvessels. Extensive fragmentation of the fibers has been noted by Papkow[3] with red corpuscles and leukocytes between the fragments. Vincent also found marked changes in the cardiac plexus, including an intense parenchymatous degeneration, with loss of the axis-cylinders. The capillaries were dilated, and the nerve cells were granular, vacuolated, and some had lost their nuclei. These nervous changes undoubtedly account for many of the features of cardiac failure in diphtheria, which up to now have seemed

[1] Beiträge zur path. Anat. u. z. allg. Path., 1912, lii, 597.
[2] Jour. Exper. Med., May, 1914, xix.
[3] Zur Frage über die Veränderungen des Herzmuskels bei Diphtherie, Wratch, 1895.

difficult of explanation. I know of no successful attempt at demonstrating the diphtheria bacillus in the myocardium, though many investigators, among them Frosch,[1] have found it in the heart's blood, in the lung, the liver, the spleen, and in lymph nodes. That it is in all likelihood present in every capillary of the heart cannot be doubted. In a number of instances diphtheria bacilli have been isolated from the vegetations upon the valvular endocardium in an ulcerative endocarditis.[2] Both the clinical picture and the microscopic findings postmortem testify to the rapid and extensive injury worked by the bacillus and its toxin. The not infrequent sudden deaths in diphtheria and its convalescence furnish another form of evidence of the damage done to the muscular and nervous cardiac structures. In very many cases the streptococcus can also be demonstrated in the blood and organs of the diphtheria patient. The feeble, almost absent apical impulse, the dulness and loss of character in the cardiac tones, the demonstrable widening of the cardiac area indicative of dilatation, and the occasional atrioventricular disassociation, all form a clinical composite that is too well known to be regarded otherwise than with dread and foreboding. Usually the toxic symptoms make their appearance about the second week of the disease. Not seldom the convalescence is the period during which grave signs of cardiac incompetency manifest themselves. The patient often vomits, the stomach rejecting everything that is introduced into it. The cardiac action may at first be rapid, but soon becomes weak and slow (50, 40, 30), and toxic heart block is not infrequently noted. Death may occur while the patient is mentally active, and is evidently due to sudden cardiac paralysis, more than possibly through crippling of the vagal centre and the terminal cardiac filaments. Occasionally the patient may live for days, seemingly pulseless (heart block). Especially if an adult he may experience the almost typical pain of an angina pectoris, reports of which in the various infectious

[1] Zeitschr. f. Hyg. u. Infectionskr., 1893, Bd. xiii, 49.

[2] Councilman, Mallory, and Pearce, Jour. Boston Soc. Med. Sci., December 18, 1900, p. 155.

diseases are increasing in frequency. More often the precordial pain is of a vague, worrisome character, grumbling and persistent, rather than the vise-like seizure of true angina. I have briefly outlined the cardiac involvements in this treacherous toxemia, which prior to the days of antitoxin reaped its annual harvest of thousands of child lives. Under the microscope the heart of a diphtheria patient shows varying grades of parenchymatous change. Fatty degeneration is the dominating process, and few diphtheria hearts escape. Marked degenerative changes have also been noted in the nerves of the cardiac plexus, suggesting strongly those found in the peripheral nerves in postdiphtheritic paralysis.[1] No doubt these changes extend to the finest nervous distribution throughout the heart structure, and presumably they are the ultimate cause of the cardiac death of diphtheritic toxemia.

The foregoing are fairly illustrative of the lesions recognized in the hearts of patients dying in or from the acute infectious diseases. Each represents a type, and other of the infections will be found to accord with its pathology and pathological physiology. Cloudy swelling, edema, vacuolization of the nuclei and cells, atrophy of the fibers, pigmentary, fibroid, fatty degeneration, fragmentation, are the important muscle lesions, common at some time to all. Typhoid fever presents Zenker's hyaline degeneration of the fibers. The cardiac nerve lesion noticed so little and their significance even less clearly understood (as in influenza, diphtheria, etc.) may all be comprehended in the different phases of fatty degeneration. The nerve changes begin usually in the myelin sheath, and the axis-cylinder often takes on a swollen and beaded appearance. The degenerative lesions in the cardiac ganglia have not, as yet, been thoroughly studied.

The point claiming final emphasis is the fact that in every case of infectious disease all the cardiac structures are injured. Some require time and rest for their rehabilitation. The vast amount of cardiac damage can never be repaired.

[1] Vincent, Arch. de Med. Exper., 1894, v.

III. Tobacco and Alcohol. *Tobacco.* By way of illustrating the phases of tobacco poisoning, I venture to cite very briefly the outline history of two interesting patients. I wish, however, to preface what I may say on the subject by the statement that I aim neither to criticize nor to trespass upon the private addictions or privileges of any man. I have, indeed, decided personal views upon the right of a citizen to lower his efficiency, and to discommode and even injure others by an indulgence which he himself freely admits is born of selfishness and bred in the neglect of the rights of one's neighbor. Yet these considerations do not properly enter into a clinical discussion. Moreover, I have long since learned that one practical demonstration is worth a volume of verbal argument.

Case I.—A few days ago I examined a patient whom I have now seen three times in the past ten years. He is a young man, F. G., aged thirty-odd years, of ordinarily good habits. He uses no alcohol, but smokes a pipe, and, on an average, a pack of cigarettes in twenty-four hours. Excepting his heart his organs are apparently healthy. I noted of him in my record for 1905 the following: "For the last few days has felt an obstruction to swallowing, not a real soreness of angina. Has a slight cough and is short of breath. Marked palpitation. These symptoms are all excited and exaggerated at once by smoking. On examination the cardiac action is rapid and thumping. Over the aortic area and in the neck are heard a loud to-and-fro murmur. The apex beat is far down and to the left. No murmurs at the apex. No arhythmia."

Under simple hygienic treatment, a little iron medication, and the withdrawal of the tobacco, in two months (May to July) the subjective symptoms entirely disappeared, as did also the aortic diastolic murmur. The systolic murmur persisted over the base of the heart.

In April, 1908, three years later, he returned with the story of having resumed his tobacco only about three weeks previously. He was smoking six to eight pipes daily, no cigarettes. My record states of him: "He is pale and peaked, has no pain, but feels smothered. Excessive palpitation. No edema." On examination I found nearly the same cardiac phenomena as on the previous occasion, except for the absence of the diastolic murmur. A loud systolic murmur was heard all over the precordia. On May 1, 1915, he consulted me again, stating that he had slowly recovered from the last attack until he was perfectly well. Has been working the year round, swimming in the summer season several miles

at a stretch without embarrassment. All subjective symptoms had disappeared and he considered himself well. About three weeks ago he began to smoke a pipe and cigarettes again. During the last two weeks has had troublesome palpitation, dizziness, weakness, and heaviness in the legs, is very nervous, his hands are blue and cold. Appetite good, sleeps well. Uses no tea, coffee, or alcohol. Smokes about a pack of cigarettes daily.

When examined he appeared far thinner than I have ever seen him. His face was flushed, his lips bluish, his arms and hands cold and cyanotic. The radial and brachial vessels were palpably distended under high tension. The whole precordia responded to the action of the cardiac systole. The rate was 120. The apex beat was well to the outside of the midclavicular line in the fifth interspace. Over the apex there was no murmur. Over the base of the heart there was a faint systolic blow, also a much more distinct diastolic murmur, heard best to the right and left of the sternum in the third interspace. Both the first and second sounds over the apex were irritable, loud, and angry. Both were overaccentuated. Over the base the second pulmonic sound was very prominent. The aortic second sound was nearly absent in the right carotid. Evidently the aortic ring was dilated, and a functional if not actual organic aortic valve insufficiency was present. There was marked dulness under the manubrium. The systolic blood-pressure was 160, the diastolic 80, yielding a pulse pressure of 80, and a cardiac overload of 50 per cent. There was no history of infectious disease.

Case II.—In November, 1914, a member of my own family, male, aged seventy-six years, experienced a severe seizure which appeared to me, as well as to a number of prominent consultants, a combination of acute toxic symptoms with an organic central nerve lesion. The patient had been under my medical supervision for fifteen years, and we based our belief upon the history, the clinical picture, and the laboratory findings. Of the toxic influence there was little room for doubt, as even the patient's urine was strong with tobacco. The organic lesion we regarded as probably a thrombo-arteritis with occlusion and stoppage, probably also secondary in its origin to the influence of the drug. In many respects the attack resembled a uremic hemiplegia. The patient was in a deep stupor, but was never completely unconscious. Against a uremia, however, were the remarkably soft brachial, radial, and temporal arteries, the known absence of sclerotic changes in the retinal vessels, the absolutely normal functioning of the kidneys, the urine free as always from albumin and casts, the slow cardiac action, and the excessively low blood-pressure, systolic 85, diastolic 50. Both patellar reflexes were completely lost. On neither side was the Babinski reflex present. This picture is almost typical of tobacco toxemia.

The heart, which had been critically examined two days before and found normal, was now distinctly enlarged and dilated. The apex beat was well advanced toward the left axillary line. The cardiac sounds were both dulled, but there was no undue relative accentuation of either sound. Slight arhythmia was present at intervals. The cardiac rate over both the base and apex was 70 immediately after the primary seizure. It then dropped to 50, where it remained for over a fortnight.

The patient's history yielded the following significant facts. He was seldom without a cigar in his mouth. During the last fifteen years, and especially during the last seven years, his left leg, and to a lesser extent his left arm had troubled him with numbness, and less freedom of motion than formerly. He complained of fulness in the occiput and sometimes of occipital pain. On relinquishing tobacco these symptoms would slowly but entirely disappear. About a month after resuming his tobacco they would again slowly but surely come into evidence. At no time could signs of arterial or cardiac or renal damage be detected, though we searched in the hope of finding something that would have weight with him. The urine was examined systematically and at short intervals, and always yielded normal characteristics. Seven and four years ago respectively cataracts were removed by Dr. W. C. Posey from the left and right eyes, and normal vision secured in both. For the past two years he has had more or less tinnitus in now one ear, now the other. This symptom seemed also to diminish markedly while tobacco was foregone. For two weeks before the recent seizure he complained of dizziness and uncertainty in walking. On the street he had such difficulty in controlling his left leg that he would constantly lurch into anyone walking on his left side. His mentality was perfect, except for a tendency to relax and become silent when not actively occupied. Two days before the seizure he was sitting at ease in an armchair. Suddenly his cigar dropped from his left hand. He was unable to rise for a few moments, and could not use either the left arm or leg. He was then helped to his feet and insisted on going down town alone to work, as it transpired, all day. On the following day Dr. Posey sent him to me with the statement that there was a haze of the vitreous humor, probably toxic, and probably due, as we both thought, to tobacco. When he came into my office the patient could walk with difficulty, owing to the embarrassment of his left side. Notwithstanding these events he presided against advice at a Thanksgiving dinner the following night, and was full of interest in the occasion. He spent the next day in bed under vigorous protest. I was called to him at 4 A.M. the next morning, and found him comatose, and the entire left side paretic, though both arm and leg began to be used before he had been lifted into bed, and he requested and guided the urinal with his right hand. During the next few hours the coma

deepened. After twenty-four hours, however, very gradually the entire picture lightened, and in two weeks he was in practical control of all his limbs and functions. A left homonymous hemianopsia then became apparent, and has persisted permanently, though with normal acuity of vision in the contracted area on the right side. There is also a marked loss of the perception of the color green near the centre of the field of vision, which, as Förster[1] and de Schweinitz[2] have emphasized, represents a frequent influence of tobacco upon the optic nerves. The customary tobacco scotomata for red and green are oval in shape and situated between the point of fixation and the blind spot.

The patellar reflexes and the blood-pressures were the last to return to normal behavior after a period of about six weeks.

At the time of the attack and for several days previous the patient had literally stunk of tobacco, not the smell of tobacco on the clothing, but of tobacco exhaled from the skin and breath of a poisoned man. We realized what was threatening, but could not persuade him to give heed. Up to the morning of the acute onset the cardiovascular system flew no signals of distress. Overnight a competent heart became a dilated, insufficient organ. The apex beat then slowly crept back to its normal position, the slight arhythmia disappeared, the first and second sounds regained their clear-cut character, and, as far as can be determined, the heart is today normally at work and furnishing no outspoken evidence of permanent damage. Both blood-pressures are now also steadily normal (130 and 80 mm. mercury).

A word remains to be said with respect to the ultimate nature of the seizure. The hemianopsia is evidently due to a thrombo-arteritis, with a sudden closing down of the middle cerebral distribution during the night of the attack or during the ten days before consciousness was fully restored. It is not of the nature of the usual tobacco amblyopia; but in the absence of any other known cause, and in the recognized toxic influence of tobacco upon the patient during years past, the drug must fairly be admitted to have been the underlying factor responsible for the arteritis, for the consequent occlusion, and the final starvation of one of the main visual centres. The paretic features involving the whole left side off and on for at least seven years must have been due to a lesion of a different location and nature, though even more certainly attributable to the tobacco. They form a by no means new syndrome. They were evidently altogether toxic, and with the removal of the drug from the body they reluctantly gave up their prey. Twice during the first forty-eight hours the patient vomited about an ounce of dark red blood.

[1] Jahresbericht der sehles Gesellschaft f. Vaterland Cultur, 1868, p. 183.

[2] The Toxic Amblyopias; Alvarenga Prize Essay; MSS. in College of Physicians of Philadelphia, 1894, p. 65.

That tobacco will cause various toxic pictures based upon the crippling of important nervous centres is well illustrated in another patient seen by me two years ago in consultation. As the result of the excessive use of tobacco, he had a fairly complete symptom-complex of tabes dorsalis in the absence of a history of syphilis. He presented Argyll-Robertson pupils, absent patellar reflexes, and very suggestive gastric crises, for which he had been operated, in the idea that he was suffering from gastric ulcer. Abstinence from tobacco for several weeks caused a return of the pupillary light accommodation, also of the patellar reflexes, as well as his first relief from abdominal pain. Eperon,[1] Uthoff,[2] Nonne,[3] and Oettinger and Strümpell[4] have all reported similar cases due to tobacco or alcohol, or to both.

I have more than once suspected, and it may easily be, that tobacco and syphilis cause the sclerosis of the posterior columns in true tabes and not syphilis alone. I have yet to discover a patient with tabes who has not partaken freely of the drug. De Schweinitz[5] has described the case of a man, aged fifty-eight years, who both smoked and drank and had typical color scotomata, side by side with the symptom-complex of tabes. There was no improvement in his ocular condition in two months, and presumably none in the tabetic picture. Here was in all likelihood an instance of true tabes associated with and perhaps partially or wholly due to tobacco poisoning. There was no obtainable history of syphilis.

The case histories of my first two patients outline the story of the influence of tobacco upon the heart, short of an autopsy. Case I is that of a youth, now a man, with a possible organic aortic valve lesion, but more likely a fairly normal heart acutely and cumulatively poisoned, though not to the extent of a complete rupture of compensation.

Case II illustrates the serious acute incompetence of a heart known to have been normal in its action immediately prior to the onset of a deeply toxic state. The tardy pulse rate, the very low systolic and diastolic blood-pressures, the arhythmia and the dilatation, in the presence of almost youthful peripheral and retinal arteries and normal urine, all speak in more graphic terms

[1] Revue med. de la Suisse romande, August, 20, No. 8.
[2] Graefe-Saemisch. Handbuch der gesammt. Augenheilkunde, xi, 2a, p. 29.
[3] Jahrbuch der Hamburgischen Staatskranken-Anstalten, II Theil, 1890, p. 91.
[4] Thése, 1882, Paris.
[5] Medical News, November 13, 1886, xlix, 551.

than any possible for me of the wickedness with which tobacco can cripple the most important mechanisms in our possession. Nor can there exist any real doubt of latent degenerative changes in a myocardium which responded in such a fashion to an acute toxemia from a drug to which the patient had long been inured.

A second attack would find the heart in a still further advancement of the destructive process, and in an even less satisfactory defensive state.

Acute tobacco poisoning of the cardiovascular system is seen in its earliest and simplest phases in the vomiting, the delirious pulse, the ice-cold extremities of the boy who has enjoyed his first cigar.

Case I of this paper pictures the combination of the features of an acute superimposed upon a chronic toxemia, just short of an explosion. Repeated attacks of cardiac incompetence such as his signify toxic processes that undoubtedly result in degenerative change.

Case II closes the story with a recital of a fulminant attack, following repeated ample warnings such as many men receive, that tobacco occasionally destroys the best we have, when they challenge its ability and power, and human like "venture to run the risk." The cerebral arteries in this case evidently suffered from the tobacco. The heart barely withstood the acute toxemia. Yet I have not up to now, overemphasized the influence of tobacco upon the cardiovascular system, because I know personally of no one whom it has actually killed, and I have no autopsy findings to present from a clear-cut tobacco case in my care. Case II described a patient who for twenty-four hours enjoyed, humanly speaking, a very scant margin of cardiac vitality. Many fatal cases of tobacco poisoning are recorded in the literature, of which I shall later cite several. I know a number of individuals who have been left in a worse state than death. A very important phase of the subject of tobacco poisoning is the insidious influence of the drug upon the arteries, now distributing its attentions throughout the entire arterial tree, again only involving some vitally important twig.

It is my confident belief that between tobacco, now in general use and abuse, and the various forms of food toxemia, can be divided the responsibility for the vast amount of arteriosclerosis that is not attributable to syphilis and old age. We have evidence and to spare, furnished by the laboratory as well as by the clinical records of such cases as we have just outlined, to show that once rid of tobacco we would have fewer instances of the gastro-intestinal apathy and food decomposition which are so often tobacco's outgrowths and coadjutors. Not a little might be said from the strictly laboratory and experimental side regarding the permanent influence of tobacco upon the heart. Harlow Brooks[1] assumes from the study of a series of "tobacco users" and autopsies upon the same that tobacco does not structurally alter or injure the heart. He quotes Hare[2] to the same effect. It does not appear, however, that his findings are at all convincing; nor does he seem to have had access to much of the recent laboratory work with respect to the injury of the cardiac structures by and due to nicotine.

One of the most reliable and conclusive studies is the investigation of C. v. Otto,[3] in which he injected a nicotine solution ($\frac{1}{10000}$) into guinea-pigs in small doses. After ten months the hearts of three of these animals were studied, about 800 serial sections being made from each. Not only the ventricular muscle, but the nerve ganglia in the auricles and the coronary sinus were scrutinized. Except for an increase in the size and weight of every nicotinized heart (as compared with the hearts of control animals) there were no macroscopic changes. Microscopically, however, wide-spread parenchymatous and interstitial changes were apparent, the former centring in the muscle fibers, the latter in the interstitial connective tissue. Fibers or whole fiber bundles had lost their form, and took the stains poorly. Fragmentation was seen in all directions. In certain cells the nucleus was very indistinct or had disappeared altogether. The proto-

[1] New York Med. Jour., April 24, 1915.
[2] Prize Essay, 1885.
[3] Virchows Archiv, September, 1911, ccv, No. 3, p. 384.

plasm appeared full of amorphous granules. The striæ of the muscle fibers gradually disappeared as the granular degeneration increased. Vacuolization of the nucleus was a frequent phenomenon. There was a marked proliferation of the fixed connective-tissue cells between the fibers, with the formation of cicatrices, especially close under the endocardium, practically never beneath the epicardium. All three coats of the cardiac bloodvessels showed involvement, though largely of the coronary branches and capillaries. Only to a slight extent did the main coronary vessels show evidence of disease. The intima of the smaller vessels showed the most marked changes, then the media, and least of all the adventitia. In the media the muscular and elastic fibers were atrophied. In this coat the change ranged from mere cloudy swelling to necrosis. The elastic fibers split up into fine fibrils. The intima showed a striking thickening and a degeneration of the elastic layer. In certain coronary twigs the intima appeared three-fourths the thickness of the media, due to hyperplasia of the connective-tissue cells. Here and there occurred a shiny hyaline mass. Occasionally the intimal changes nearly occluded the lumen.

The nerve ganglia presented extensive, definite degenerative processes. The Nissl bodies were greatly diminished in number in the larger nerve cells and replaced by vacuoles. Nerve cells of unusual midsizes (between the normal large and small) were in decided evidence. The bloodvessels surrounding the ganglia showed degenerative changes similar to those described above. The vessels running in and through the ganglion itself showed swelling of the endothelial cells, but never was there an encroachment upon the lumen to the extent of stoppage.

Other studies that contain much of similar interest are those of Zebrowski,[1] Nicolai,[2] Pawinski,[3] and of Cannon, Aub, and Binger.[4] In the latter it is demonstrated that nicotine actively stimulates the adrenal secretion, and may thus exert an indirect influence

[1] Przeglad lekarski, 1908.
[2] Zeitschr. f. exper. Path. u. Therap., 1908, viii.
[3] Zeitschr. f. klin. Med., July, 1914, lxxx, 284–306.
[4] Jour. Pharmacol. and Exper. Therap., March, 1912, p. 381.

upon the vessels through the adrenals, in addition to its own direct poisoning of the cardiovascular structures.

I wish at this time simply to submit my own fairly eloquent clinical finding, and those of others. Tobacco has struck very deeply into the vitals of the home in which I was born, and I would like to furnish the members of my profession with evidence sufficient to justify their refusing to prescribe certain injury, and possible catastrophe, that will come, if at all, as stealthily as it certainly will with permanent crippling and harm. If it had not been for regrettable advice on the part of physicians, Case II could have been spared his catastrophe. In the light of such clinical pictures and the autopsy findings of Favarger, yet to be detailed, one can hardly sympathize with Brooks in his assertion that "if experimentatoin, pharmacology, and clinical observation have taught one single fact about the action of tobacco, it is that its effects, while occasionally very dangerous, are evanescent." Rather must we conclude that while the drug simulates a temporary effect, it is working silent, permanent injury beneath the surface. Only yesterday a physician said to the writer, "I have had to give up my cigars. I knew they were hurting me. But even though I stopped smoking days ago I am still short of breath and have pain almost constantly in my heart." This physician's dyspnea is cardiac dyspnea, and implies insufficiency of the cardiac muscle, how temporary or how permanent the event will tell. Tobacco is an anesthetic, a narcotic, it quiets and soothes irritable nerves just as do alcohol and opium, and in an identical way. It exacts much more certain cardiovascular toll, which some of us cannot afford to pay. There seems to be ample evidence for the belief that it stimulates and irritates and later paralyzes the vagus, and also the sympathetic (including the autonomic) system. This is apart from a directly poisonous action upon the heart muscle and the media and interna of the vessels.

I am accumulating a considerable amount of clinical evidence indicating that the children of the tobacco user and his tobacco-absorbing wife also pay a cardiovascular toll in the form of a tendency to fibrous and leathery bloodvessels that have often

enough been attributed to heredity, but seldom or never to its exact phase. This is, however, a subject for discussion by itself, so more thereof at another time and on another occasion.

Fraenkel-Hochwart[1] has experimented with healthy smokers and non-smokers with respect to the influence of tobacco-laden air (smoked by others or smoked artificially). Out of 62 separate experiments on persons whose pulse, respiratory rate, blood-pressure, were taken at different, frequent intervals, he found that only two subjects failed to show marked changes in blood-pressure. Two individuals, both moderate smokers, showed no marked reaction while in the smoke-laden air, but ten minutes after leaving the room showed a violent and excessive fall in pressure, with slowing of the pulse in both. Of 28 adults who sat twenty minutes in a tobacco smoke-filled room, 5 showed little reaction. Of the remaining 23, 11 experienced a marked fall of blood-pressure. The pulse rate was unchanged in 5 of these, increased in 4, and slowed in 2. In 5 of 10 persons the blood-pressure fell more markedly when they themselves were actively smoking than when they were passive in the tobacco smoke. In another article, Fraenkel-Hochwart[2] also refers to the well-recognized association of tobacco with intermittent claudication, to the production of the arteriosclerosis underlying the condition, and to the relief from symptoms which not infrequently follows the withdrawal of the drug.

John[3] has carried out a careful series of observations, and finds that two moderately strong cigars will cause typical changes in the blood-pressure. During the smoking there is an increase in the diastolic pressure, a primary rise in the systolic pressure, followed by a decided fall. These variations from normal last about two hours after the smoking has been discontinued.

Favarger,[4] to whom I have already referred, cites a most convincing series of cases observed by himself including fatal cases of both acute and chronic tobacco poisoning. He noted repeatedly

[1] Deutsch. Zeitschr. f. Nervenheilk., 1913, Nos. 47 and 48.
[2] Deutsch. med. Woch., December 4, 1911.
[3] Zeitschr. f. Exper. Path. u. Therap., September 16, 1913, Bd. xiv, Heft 2, p. 332.
[4] Wien. klin. Woch., April 23, 1914, xxvii, 497.

marked and typical cardiac disturbances, including arhythmia, bradycardia or tachycardia, precordial oppression, dyspnea, myocardial insufficiency (dilatation), cardiac asthma, Cheyne-Stokes respiration, cyanosis, and in 6 cases fatal cardiac paralysis. He obtained an autopsy in one striking acute-chronic case and found (Paltauf operating) cardiac "dilatation and a high degree of fatty degeneration throughout the heart." There was also found at the autopsy an extensive hemorrhage into the bowel, evidently toxic, and probably of the same nature as that which occurred from the stomach in my Case II. He emphasizes the fact that many cases in his experience have shown tobacco myocardial insufficiency in the entire absence of demonstrable sclerosis. I have already called attention to this feature of my second case.

L. Mitchell Bruce,[1] in the Lettsomian lecture, states as his experience that "In young men with hearts still structurally sound, the uncomplicated effects of tobacco, as presented clinically are palpitation in every instance; a sense of irregular action, poststernal oppression and pain in one-half the cases; and in 1 out of every 8 either angina or uncomfortable sensations in the left arm; faintness or actual faints in one-third of the cases; giddiness and a feeling of impending death in a smaller proportion; the pulse tension with insignificant exceptions is low."

I shall further merely mention the important investigations of W. E. Lee,[2] Clerc and Pezzi,[3] Bruce, Miller, and Hooker,[4] and C. Fleig.[5] All of the foregoing have demonstrated vasoconstriction as the result of tobacco exposure. The action upon the heart and bloodvessels is both central and peripheral. Fleig has subjected the young of guinea-pigs to tobacco smoke. Not one of the number developed into a normal or healthy animal. If the pregnant mother was exposed to the smoke the young were either born dead or else were dwarfed and far beneath the normal birthweight. Any individual can execute a similar experiment with

[1] British Med. Jour., March 23, 1901.
[2] Quarterly Jour. Exper. Med., London, 1908, i, 335.
[3] Compt.-rend. Soc. de Biol., lxxii, 316.
[4] Amer. Jour. Physiol., April, 1909, p. 104.
[5] Compt.-rend. Hebd., April, 1908.

the seedling of beans or peas, growing one lot in a jar over clean water, and a second lot from the same picking over a jar into (not on) the water of which have been blown four or five mouthfuls of tobacco smoke. The tobacco poisoned growths are stunted and pitiful. Tobacco strikes at the heart of things, whether plant or animal. One of the most typical instances of violent and agonizing angina pectoris I ever witnessed was in a young man of thirty, saturated with tobacco. For over fifteen years he has been free from pain, and is still living and well, without tobacco. Most of the instances of so-called pseudo-angina in males are due to this drug. I am convinced that many if not all of the instances of of pseudo-angina are examples of toxic involvement either of the ganglia of the heart or of the nerves of the cardiac plexus, and that when there is an opportunity of exhaustive microscopic post-mortem study it will prove fruitful along these lines. Not one can properly be called a neurosis. The pain is too constant for it to be explained on the basis of coronary constriction, especially since the effect of tobacco is eventually vasodilation after its first temporary influence. In any event tobacco's action on the circulatory system is swift and certain. Even in the absence of high diastolic tension in the habitue it tends toward intravascular disease, of the heart, of the brain, or of the entire economy, the latter forming the rule. From the evidence secured in my own cases, as well as the more definite demonstration in the long-sought human autopsy of Favarger, and the laboratory work of v. Otto, it seems fair to conclude that degenerative processes are at work in every tobacco poisoned heart.

Alcohol. Of the clinical picture of acute alcoholism nothing need be said in this connection. We know it too well, from the glimpse seen in the baby who is receiving a drop at a time through the breast of its mother, or when actually placed in the bottle; to the child who receives at the table "just a taste of beer," on to the freshman who learns to drink boldly at his first college supper; and to the "good fellow" who lies limp under the banquet table. There are, we believe, fewer and fewer of him. I refer to not one of these in the brief description which follows. My discussion is

solely of the therapeutic use of alcohol, almost the twin of tobacco in its anesthetic and narcotic effect. We need not waste time in discussing its lack of claim to a food value, in any true sense of the term. This lack has been demonstrated beyond all peradventure, and has been accepted as a working principle in all of the foremost laboratories. (A. E. Taylor, Winfield S. Hall *et al.*) Backmann, of Upsala, presented in 1907 before the Alcohol Congress at Stockholm the results of his experiments with the drug on the isolated heart of the rabbit. He called attention to the fact that Locke and others had demonstrated the actual food value of grape and fruit sugars and their power to gradually augment the contractions of the isolated heart. In striking contrast he showed the action of alcohol when even the most dilute solutions (0.0025 to 0.5 per cent.) were perfused through the heart vessels after the vigor of the organ had been appreciably diminished. If the alcohol was used in strength sufficient to produce any noticeable effect, it always caused a diminution in the strength of the contractions, with arhythmia, also a slowing of the cardiac action. When replaced by a (0.5 per cent.) solution of sugar in most cases there was a positive restitution of cardiac power and capacity for work. I shall consider only the clinical and laboratory indications and contraindications for the medicinal use of the drug which has so recently and so suddenly been transferred from the class of cardiac stimulants and tonics to that of the cardiac depressants and poisons. At a recent meeting called for the consideration of the medicamental use of alcohol a number of experienced clinicians and consultants in internal medicine took part in the discussion, and only one, the oldest in years and experience, made the slightest reference to its influence upon the cardiovascular system, and he only in passing. Not one seemed to lay any stress upon the mass of clinical and laboratory evidence ready at hand in the matter of the physiological action of alcohol in small doses and large upon the heart, upon the cardiac system of nerves, and upon the vasomotor nervous system.

We do not know that alcohol produces arteriosclerosis, whether

used moderately or immoderately. We do know that in small doses and large in continued use it soon depresses and then paralyzes the vasomotor nerves. We also know that tobacco does indeed cause arteriosclerosis, and that the use of alcohol practically implies the craving for tobacco. To put the same truth a little less pugnaciously, very seldom is an individual discovered who uses alcohol in any form or in any dosage who does not also use tobacco, whatever his own explanation of the coincidence. Other excesses in food and venery are closely associated with alcoholism and the tobacco habit, that tend equally toward sclerotic vessels and myocardial disease. It is impossible, therefore, either to indict alcohol on the score of directly producing arteriosclerosis, or to completely relieve it of either a direct contributory or indirect responsibility for much of the rapidly increasing cardiovascular disease. In New York State eight years ago (1909) there were 23,000 deaths from cardiovascular disease, and only 17,000 deaths from tuberculosis. During 1914, 2205 physicians died in the United States and Canada, an approximate death-rate of 14.41 per 1000. The chief causes of death were the cardiovascular diseases. In Philadelphia during 1914 there was a general increase of 400 deaths (7 per cent. from organic heart disease over the total of 1913. Of apoplexy and paresis there was an increase of 54 deaths (9 per cent.) These are significant figures when we realize that the most active causes of cardiovascular disease are the trio, so often found in company, tobacco, alcohol, and syphilis, in the rich and poor, in the highly respectable and in the outcast.

It is only fair, however, to exonerate the drug alcohol from a contribution to the sclerotic total when used by the physician in therapeutic dosage, if there be any such thing. It harms the vessels by injuring their vasomotor control; though its really pernicious influence under such circumstances is upon the various structures of the heart.

I have spoken of alcohol as tobacco's near twin. It is such in its primary action, in small, and in certain respects also in large doses. Clinically, both alcohol in small doses and tobacco smoked

or inhaled *at first* stimulate the heart directly and increase its rate, force, and volume output. Both drugs *at first and for a brief interval* raise both the systolic and diastolic blood-pressures, the systolic as the result of direct stimulation of the heart muscle, the diastolic through stimulation of the vasomotor nerves. To the above extent the laboratory results accord with the clinical findings in the similarity of the two drugs in their action upon the heart and vessels. Dixon[1] has shown, and anyone can confirm his animal experiments in the healthy or the sick human subject, that in small doses alcohol at first slightly stimulates the cardiac systole. Whether this result is attained through a depressant action upon the vagus, or a stimulant influence upon the sympathetic nerves, or upon the cardiac muscle, is uncertain. Both the systolic and the diastolic pressures are momentarily slightly elevated, the splanchnic vessels being constricted, and the peripheral capillaries dilated. Probably as a consequence of all these factors the heart gains the briefest and most temporary lift, as it were. Therein lies the sole justification for the therapeutic use of alcohol, at any time or in any circumstance. Hot water and ammonia, or hot water alone will do all these things better than alcohol, and without any secondary effects that more than undo the benefit that has been conferred. Within a few brief minutes (usually not more than five or ten) alcohol becomes tobacco's half-twin only for the time being. It no longer raises the diastolic pressure. No longer does it constrict the splanchnic vessels. It still resembles tobacco, however, in that instead of stimulating the cardiac muscle or nerves it now depresses both. This becomes more evident, even if small dosage is continued, from the sometimes over-rapid, sometimes very slow, feeble cardiac action, the lessened output, the manifest signs of cardiac dilatation, the not infrequent auricular fibrillation, the arhythmias due to other factors than interrupted conduction, and the systemic signs of imperfect compensation. The systolic and diastolic pressures fall together far below their starting-point as the result of cardiac and vasomotor crippling, and this toxic effect continues with

[1] Jour. of Physiol., 1906–1907, xxv, 346–361.

increasing tendency to depression of the cardiac forces until the drug is withdrawn. If large doses have been administered (as is usually the case in emergency as well as in continued treatment) the depressant influence is active from the beginning. Tobacco in its chronic and in its overwhelming and fulminant poisonings also paralyzes the heart and vasomotor system, and again re-establishes its full cardiovascular twinship to alcohol.

There is an abundance of reliable evidence to show that the administration of alcohol lowers the vital resistance to bacterial infections in at least two ways. It diminishes the power of the human economy to marshal its phagocytes when and where it pleases. These are all important defenses in certain forms of bacteriemia, and probably by their activity or through their inaction they often decide the issue for recovery or death. Alcohol also lowers the ability of the body to manufacture the antitoxins requisite to combat the infections which work mainly as toxemias. The only conceivable occasion on which the drug could assist in a grave toxemia would be in such an infection as typhoid fever, occurring in a strong, robust individual of high antitoxic resisting power, in whom there is too wholesale a destruction of bacteria in the tissues, with danger that the patient may poison himself to death through the very process that usually works the cure. But in the vast majority of typhoid patients, indeed in all of the asthenic type, such a danger is out of the question. Every germ killed is one more danger set aside. The patient is a rare exception in whom the natural defensive forces may be wasted with impunity. Hence there are a few physicians approximating above or below forty years of age who feel that a place remains for alcohol in the pharmacopœia of the well-read and conscientious physician, except as an emergency stimulant, and then only in minimal dosage, which does not mean a half-ounce or an ounce at intervals of a few hours.

Again, it is certain that the action of alcohol is the same upon the cardiovascular system of the old as upon that of the young, except that in the former it finds tissues less normal and recuperative, and much less prepared to withstand its toxic and depressing

effects. Few old people have a systolic pressure that approximates the normal. Alcohol in any dosage pushes it still lower. Only an occasional senile body has young arteries and veins. Alcohol lowers the tone of the cardiac muscle and its extension in the arterial muscular coat even more certainly in the aged than in the young. The senile individual needs every force that will sustain and enhance a failing circulation. To give him alcohol is to deplete his reserve store. Why then, let us ask, do some still venture to say "In infections and in bacteriemias and in toxemias like typhoid fever" (I am not sure that I am quoting verbatim from the meeting already referred to) "alcohol does do good—I know what I say because I have been there"?

One is almost at a loss to reply to such an assertion with the consideration and patience that are obligatory in a scientific discussion. Some have been in the Arctic regions and have honestly thought they have seen that which they did not see. Moreover, one thing can be charitably said for all of us who cheerfully, and as we thought successfully, used alcohol in our work ten years ago, and today are just as cheerily and just as confidently laying it aside as a no longer doubtful poison and as a destroyer of living tissue. We were wrong then; we are more nearly right today. Let us err on the safe side until we learn whether there be a midposition struck when the pendulum comes to rest. It must also be admitted that one individual can secure results with a medicament which another cannot; else medical history is full of clinical investigators whom one would like to, but dare not trust. This refuge of an isolated success is not open to the alcohol advocate, however, since we were all at his side a few years ago. Only he has failed to read the signs of the times and to move on a little. I think the real secret of the alcohol advocacy and the undoubtedly honest conviction of the alcohol advocate is to be discovered in three subtleties in his makeup. First, he is always and invariably a so-called "moderate drinker." Second, he clings fast to the threadbare theory that the individual has a right to be a moderate drinker, whether it injures him, his posterity, his neighbor (by example), and the community (by the

lowering of his own efficiency) or not. Third, and most potent of all, the older one becomes the more firmly he gets set in a groove, and the more difficult it is to persuade him that there is pleasant pasture outside his narrow confines. "He has been there," and is content! So have we, and have learned better things. We agreed with him on a given point ten years ago. We differ on that identical point today. Moreover, we base our variance on bedside findings and on laboratory demonstration, on both human beings and on the lower animals. He really wasn't there at all! Nor were we! We both thought we were! He remains reluctant, for the reasons submitted, to follow us out of the old groove. But to maintain his position he must admit an ignorance of, or an unwillingness to examine and weigh evidence that will convict him of error, provided he employs the same fair methods of estimating that characterize his judgments in other matters.

The physiological effect of alcohol is better comprehended by the lay public today than by the average medical man, if one can judge by the tide that is sweeping over the country. The first awakening and the first outspoken testimony came into evidence only a week ago when 700 of the physicians of Pennsylvania openly took their stand for the right of a community to determine by vote whether its citizens should or should not barter away their health in exchange for avoidable cardiovascular disease. The next advance will be the ranging of the national medical body on the side of the disuse of a drug which its members have heretofore freely employed in good faith, but which they are now forced to recognize as in any dosage a cardiovascular nerve and muscle poison, a tissue destroyer, and an economic harm.

Now for the evidence, in very brief. I have in fairness already cited Dixon's animal experiments to illustrate the general agreement that the first fleeting influence of small doses of alcohol on non-alcoholics is stimulant. I have also stated the fact, based on clinical and laboratory study that this action is promptly followed by a vigorous and permanent cardiac and vasomotor depression, *i. e.*, weakening. In all toxemias, and probably in all infections

that act directly as bacteriemias, the heart and vessels constitute the main reliance of the body with respect to maintaining the fight against exhaustion. This principle holds peculiarly true in the pneumonias, in typhoid fever, in tuberculosis, in diphtheria, in scarlet fever, and, to a lesser extent, in the true rheumatic states. It is in this class of heart-beset infections, in certain of which the blood carries bacteria and toxins to every cardiac and vascular muscle and nerve cell, I repeat, it is particularly true in this group of bacterial diseases the alcohol advocates are maintaining their right to use a cardiovascular depressant and poison.

Ewald,[1] though not himself a teetotaler, has discontinued the use of alcohol in the infectious diseases as being useless, either in reducing temperature, or as a hypnotic, or as a bactericide. He finds that it reduces the resisting power of the blood. He is convinced also that camphor, strychnine, and caffein answer every purpose for which alcohol is used internally, and accomplish better results.

As to the clinical successes of those who have recently spoken for the retention of alcohol as a medicament, Miller[2] gravely reminds us that Laennec had a specific for pneumonia in tartar emetic, that Petrescu treated 2215 pneumonia patients with large doses of digitalis and experienced a mortality of 1.7 per cent., and that Aufrecht reported a series of 379 cases of pneumonia cases treated hypodermically with quinin with a mortality of only 2.6 per cent. Miller also quotes Dennig, Hindelang, and Grünbaum[3] with respect to their experiments in administering alcohol (in doses corresponding to 6 c.c. of absolute alcohol in man) to dogs suffering from various infections. In all there was a fleeting rise in the blood-pressure; then in five minutes a marked fall which persisted for forty-five minutes. When larger doses were given the primary rise in blood-pressure did not appear. Sixty-two febrile human subjects, mostly suffer-

[1] Medizinische Klinik, August 3, 1913, ix, No. 31.
[2] Jour. Amer. Med. Assn., December 10, 1910, p. 2034.
[3] Deutsch. Archiv f. klin. Med., 1909, xxvi, 153.

ing from acute infections, were then given graded doses of absolute alcohol well diluted. The first ten, including three pneumonia patients, were given 6 to 10 c.c.; and in all but three both the systolic and diastolic pressures (the indicators of cardiac muscle and of vasomotor tone respectively) were reduced one and one-half to two hours. Larger doses were given to the remaining groups and still more prompt and positive evidences of cardiovascular depression and of diminished cardiac output were obtained. Galli[1] urges that in all cases of cardiovascular disease disease alcohol can and should be withdrawn completely and at once. He quotes Hernung to the same effect. Galli's researches at the Bacelli Clinic have convinced him that even in healthy persons alcohol tends to weaken and dilate the heart, and to lower the blood-pressure. He has confirmed these studies by Roentgen examinations by the orthodiagraphic method, which showed that the heart often increased as much as 2 c.c. in width within a few hours, even with the patient at complete rest. The blood-pressure rose during the first ten minutes, and then fell permanently an average of 30 mm. mercury.

Brooks[2] concludes from his experiments on dogs, administering 10 c.c. and ascending doses of alcohol by the mouth, by intravenous injection, and by gastric fistula, that the drug causes a marked preliminary rise in blood-pressure with "increased amplitude and a constant or slightly slowed rhythm of heart beat." This rise in pressure disappears in five or ten minutes, and is followed by a gradual progressive lowering of blood-pressure, with decrease in amplitude and rapidity of the heart rate. The latter he regards as the "true pharmacological action of alcohol on the blood-pressure of the intact, unanesthetized animal."

Kochmann[3] and Rosenfeld[4] agree substantially with Dixon (already cited) and the foregoing that alcohol at first stimulates very briefly, if at all.

[1] Riforma Medica, 1907, xxii, No. 48.
[2] Hull Laboratory of Experimental Therapeutics, University of Chicago, Jour. Amer. Med. Assn., July 30, 1910, p. 372.
[3] Archiv. Internat. de Pharmakodynamie et de Therapie, 1904, xiii, 329.
[4] Abstr. Centralbl. f. Innere Med., 1907, xxviii, 853.

Laitinen[1] represents an army of laboratory workers, practically all of whom agree that in any dosage whatsoever alcohol lowers the bactericidal power of the blood as well as the ability of the animal to combat a toxemia by the manufacture and use of antitoxin.

Even outside the body it now becomes a question whether or not alcohol has more than a negligible antiseptic power in any concentration or in any dilution. Certainly in the form of absolute alcohol it has none. In Sir W. Watson Cheyne's plate-cell experiments[2] carried on during the present European war, he has inoculated cells with pus organisms, then treated them thoroughly with alcohol, and grown from them luxuriant cultures, as shown in his illustration. Of the possibility of establishing in certain individuals the alcohol habit, I will simply say that I see occasionally an educated, refined woman who has for years fought the taste, established long ago during her treatment for typhoid fever by one of the Fellows of this College. She had never tasted whisky before. Since her convalescence from the typhoid, and not until a year ago had a twelvemonth passed by without repeated intoxications, now with whisky, now with alcoholic proprietary medicines, or any form of alcohol she could secure. I think she has finally won her fight, but it has cost her many an hour of physical and mental distress and years of invalidism, with a dilated heart, a crippled vasomotor system, and the prospect of permanent cardiovascular disability.

Finally with reference to the influence of alcohol through heredity, of course, through the cardiovascular blood supply and the germ cell. Stockard of the Cornell University Medical School[3] has shown that the germ cells of male laboratory animals can be so injured by the inhalation of fumes of alcohol that when mated with healthy alcohol-free females the offspring are physically imperfect and defective in development. In a subsequent study[4]

[1] Zeitschrift f. Hyg. u. Infectionskr., 1907–1908, lxiii, 139.
[2] Lancet, February 27, 1915.
[3] Archiv f. Entwicklungs. d. Organ., 1912, xxv; also Archives of Internal Medicine, 1912, x, 369.
[4] Proc. Soc. Exper. Biol. and Med., 1914, xi, 136.

he has demonstrated that a tendency to these defects is transmitted through several generations. Certain generations may be passed over without structural defect being apparent, and then without warning aplasias will again occur, such as the complete absence of malformation of the eyes, or of the optic chiasm, of a complete defective development of several members of a litter. These animals undoubtedly show the results of a poisoning of every tissue in the germ cell including its circulatory system and vascular blood supply. In certain of the defective progeny there has actually been found an hypoplastic cardiovascular apparatus. I have repeatedly seen the same under- and defective development in the children of human alcoholics, and have learned to expect to find in them cardiovascular lesions and insufficiencies.

Schweighofer,[1] in reporting his Salzburg investigation, has recorded a suggestive and interesting lesson in alcohol heredity in the human being. A healthy woman married a healthy man and bore him three healthy children. After his death she married a confirmed alcoholic and bore him three children, one of whom persisted in infantilism, and a second and third became social degenerates and drunkards. Two of these children became tuberculous, the first instances of the disease in the family. The woman married a third time and bore to a healthy husband physically sound children. Beside such a demonstration Karl Pearson's whole mass of argument seems puerile. Adami[2] concludes his address to the Canadian Medical Society as follows: "When it is being taught that parents may subject themselves to intoxications and infections, and that their offspring in their bodies and in their health pay no penalty—then I hold that it is the duty of the physician to tell the truth as he knows it, and to express in clear, unveiled language the basis of his belief." And a little earlier in the same address, "We have long observed that intoxicants affecting the body of the parent are liable also to affect the germ cells."

[1] Alcohol u. Nachkommensch. in das Oesterreisch. Sanitätsverein, 1912,
[2] Lancet, November 2, 1912.

Bertholet[1] has reported his examination of the testicles of 75 men, of whom 39 had used alcohol excessively, and the majority of whom died about middle life. In 37 out of the 39 alcoholics there was wide-spread atrophy of the testicular parenchyma, and a marked replacement fibrosis, altogether differing from the changes of senility.

I have touched in turn upon the several forms of clinical and laboratory evidence for and against the use of alcohol in medicine; first, its availability as a temporary cardiac support; second, the certainty of its prompt depressant and poisonous action; third, the possibility of initiating a harmful drug habit in the patient; and finally, the disputed, but well-demonstrated cardiovascular and germ cell hereditary influence. All of these are factors which base their force as arguments upon cardiovascular considerations.

I have omitted for obvious reasons all reference to experimental studies made upon anesthetized animals. Nearly all of the advocates of the continued stimulant action of alcohol base their convictions upon experimental work carried out upon animals already drunk with some actively anesthetic form of alcohol. Experiments of this type are neither trustworthy nor intelligent. As a matter of fact, ethyl alcohol behaves in many ways like chloroform, one of the anesthetics used. Surely I have cited a sufficient amount of well authenticated experiment and of clinical study by masters in their respective fields to attract the attention of even those who "have been there," and who yield, if at all, still struggling, only as the avalanche rolls over them.

Let me simply add my own experience, namely, that since becoming convinced of the injury I was doing my patients with alcohol, and the lack of need for its use in any condition that comes under the care of the physician, I have not prescribed or administered a drop of the drug except as the inevitable vehicle and solvent. Meanwhile I have seen pneumonia and typhoid and pure cardiovascular conditions recover with greater promptness

[1] Centralblatt f. Allg. Path., 1909, xx, 1062.

than when treated with alcohol. Moreover, I have felt confident under the new regimen that I have hurried no one into eternity, as I may easily have under the old.

A study of the cardiovascular poisons is altogether incomplete in the lack of consideration of an excessive production of the internal secretions such as that of the thyroid and adrenal glands, of coffee and tea, of phosphorus, nitroglycerin, pilocarpin, chloroform, illuminating gas, and many other substances that will not crowd into the time or space at my command. I have called attention to the three groups that come closest home to the every-day citizen and his friend the general practitioner, and in confining myself to their study I trust I will be misunderstood by none. The other important and interesting fields have not been overlooked. There is much to be developed in the near future concerning the physiology of the heart, especially on its nervous side. Let us have no unscientific regret if the next generation of heart students shall by even more real advances sweep much that we seem to have discovered away.

DISCUSSION

Dr. H. A. Hare: Sometimes in meetings of American associations I regret that the custom is not carried out which is so constantly adhered to in English medical societies, namely, to follow the habits of our brothers, the lawyers who, at least, in court, attack one another vigorously. Medical men in England attack the paper of a colleague without the slightest hesitation. Indeed, I know of no branch of the profession in which the same thing is done in this country, unless it be possibly among the gynecologists, and that possibly among the gynecologists of twenty years ago rather than today. Anything that I say tonight, it goes without saying, is not said with any intention to give offense. I have felt, however, that I might be inert or speak: that I might fail to discuss the paper, because in so many respects it seems to me so utterly erroneous that I would perhaps dignify it by discussion. Or, on the other hand, if I did not discuss it, there would be a possibility of this paper going before the community and being quoted as a paper read before the College of Physicians of Philadelphia, a learned body, and it would appear that no one had for a moment thought of gainsaying its statements.

Dr. Willson, under the title of a paper on heart disease, has really read an attack on alcohol as a drug.

Now, if I may be pardoned for saying so, the first mistake in Dr. Willson's paper is the mistake of making sweeping statements without the slightest justification for many of them, and some of them in direct controversion to known laws of physiology and pathology. To state, for example, that in the early stage of the influence of alcohol this drug stimulates the circulation by stimulating the vagus is to show an entire ignorance of what every second-year student in medicine knows—that the function of the vagus is inhibitory and that in its action it decreases functional activity of the heart rather than increases it. When the statement is made that alcohol produces arteriosclerosis and arterial spasm and in the same breath the assertion is made absolutely that alcohol depresses the entire vasomotor apparatus, it is difficult to agree, for it is not easy to see how a drug can produce a rise of blood-pressure at the same time that it is producing a lowering of blood-pressure by depressing the vascular system in general. Some years ago I read before this College a paper on the Brand bath in typhoid fever. I still think I was right, but during the discussion of that paper Dr. William Osler said that it was one of the best presentations he had ever seen of how a lot of statistics could be used to prove the wrong point. I am inclined to think that some of these statistics tonight have been brought together from hither and yon and presented in such a way as to give an erroneous impression. In the first place, the reader of the paper does not seem to be familiar with what physiologists and pharmacologists recognize as the true physiological action of alcohol. When some of us were students we were taught that alcohol was a cardiovascular stimulant; we now know that it is not. Pharmacologists tell us that it is always a depressant to every tissue if used in any dose. So far as its circulatory action is concerned alcohol in moderate amounts does not act as a stimulant or as a depressant, but it equalizes the circulation. In many cases of disease in which we find the peripheral portion of the body lacking in a proper supply of blood, which means that there must be congestion of the internal viscera, alcohol by dilating the peripheral capillaries and contracting the central capillaries equalizes the circulation and makes the finger-tips, the ears and nose of normal appearance, and if we could see the internal organs we should see them of normal appearance also.

Now I believe that this matter of attacking alcohol does a great deal of harm because it produces an entirely erroneous impression about the drug. I believe there is no drug that has physiological power, which if wrongly used, will not also have the power to do harm. In a recent meeting of the County Medical Society a gentleman who read one of the

papers said that alcohol was always contra-indicated in tuberculosis. Any one practising medicine but six months would know that this statement is too sweeping to bear any weight and yet taken from the proceedings of a society and published under certain circumstances it might do harm. Every practitioner of medicine knows that while alcohol is harmful in miliary tuberculosis, in fibroid phthisis with cough interfering with digestion, the administration of alcohol is the administration of a food which is burnt up in the body, which lends energy to that body which stimulates digestion, and which if given in the proper form may even help him to expectorate the material which is in the cavities.

What is intended, I take it, is not a paper advocating alcohol, and not a paper condemning alcohol, but the presentation before this College of a paper which recognizes that when alcohol is abused it does harm; when used rightly, it has definite, specific and often a very valuable place in medicine. This is true in diabetes mellitus in which disease, in certain cases, alcohol burnt up in the body possesses a distinct food value.

Now the reader of the paper has gone one step further. He made the dogmatic statement that *all*—I think he said all—researches show that alcohol decreases the ability of the blood to combat infection. I will be equally dogmatic. They don't do anything of the kind. On the contrary, there are researches that show it increases the ability of the body to protect itself in certain instances. Some time ago I presented a paper before the Association of American Physicians in which I presented the results of research to the effect that in typhoid fever and tuberculosis, alcohol in proper doses increases very materially the bacteriolytic action of the blood. Had I known that this aspect of the question would come up tonight I would have brought some charts with me. The technic by which studies were made was according to directions given by Dr. Simon Flexner. The bacteriologist who did the work did not know that the patients were taking alcohol. In every instance the bacteriolytic power of the blood was remarkedly increased by the proper use of alcohol.

With one point that Dr. Willson made I agree—that the crusade which has been waged against alcohol in the profession has diminished the size of the dose that many physicians now give. My distinguished preceptor, Dr. H. C. Wood, recommended doses sometimes as large as a pint during the day and claimed that he and others had seen excellent results, and within the last six months Dr. Abraham Jacobi, of New York, a man with an enormous experience, and possibly now that Dr. Weir Mitchell has gone, the most honored physician in the United States, has written a paper in which he lauds the freest administration of alcohol in combating infectious diseases.

I do not want to hear a paper in which all the evidence is summed up

against a thing. Why does not Dr. Willson say that some men discredit the alcohol but that others find it a useful agent, and weigh the facts? That is the sort of scientific discussion this College wants, and to views obtained only in this way will it adhere.

Dr. H. C. Wood: There are several loose expressions in Dr. Willson's paper which I do not think should be allowed to go uncorrected. He speaks of the "cardiovascular action" of drugs. It is well known that a drug may have one action upon the heart and an opposite action upon the blood-pressure. Because a drug lowers blood-pressure is no proof that it depresses the heart, and *vice versa*. Pharmacologists always separate these two actions and study the effect of the drug upon the heart as distinct from its effect upon the bloodvessels. If he had made this distinction he would probably not have fallen into the error of comparing alcohol to nicotine in its physiological action. It is hard to imagine two drugs more widely different in physiological effect than alcohol and nicotine. To a pharmacologist to compare the action of nicotine to that of alcohol is almost ridiculous.

Regarding the experimental studies quoted by Dr. Willson I am a little surprised at the conclusions he drew from those experiments. In the first place, he fails to make sharp the distinction between the therapeutic and the toxic dose of alcohol. He speaks of the secondary results of alcohol as if the depressant effect followed when therapeutic quantities were given; whereas, I understand that the depressant results are the effect of toxic doses. Dr. Willson quotes the experiments of Dr. Dixon, but neglected to say that Dixon reached the conclusion that alcohol acted as a foodstuff for the heart. He quotes Dr. Kochmann. It is a long time since I read Kochmann's paper, but the impression made upon my mind at that time was that he regarded alcohol in proper dosage as a stimulant to the heart muscle. Regarding the experiments by Dr. Hoyt in the laboratories, in which I was then at the head, I can speak with a little more confidence because I saw these experiments myself and had considerable to say in the management of them. I may say that the conclusions reached in those experiments were not represented in Dr. Willson's statement of a primary stimulation and a secondary depression. In a paper published by the International Academy of Science it is stated that in less than one-half of 1 per cent. alcohol increases the power of the heart muscle. Nothing is said about a secondary depression in small doses of alcohol but it is pointed out that large doses of alcohol do depress the heart muscle. I do not think there is any reliable scientific evidence that the secondary effect of these small doses is a depressant action upon the heart muscle.

It is hardly part of the subject to refer to the effect of alcohol upon the

offspring. I do not quite see the connection between eugenics and cardiac disease, but since Dr. Willson has brought up the subject I may refer to the fact, probably known to many of us, that Professor Carl Pearson, one of the most famous sociologists of England, but not a medical man, maintains that there is no evidence that alcohol does affect the offspring; that is, that the children of alcoholics are in no way different in the long run from the children of non-alcoholics. To be sure, his conclusions are not universally accepted; but it is at least rather sweeping to say that all scientists agree that the children of alcoholics are universally degenerates.

One further statement which I think is most astonishing is that Dr. Willson never prescribes alcohol in any form. I must confess that I do not see how a man can practise medicine without prescribing alcohol. He would not be able to give tincture of digitalis, of nux vomica, or a host of other drugs. The compound tincture of gentian which 80 or 90 per cent. of us are in the habit of using as a bitter tonic probably owes a large proportion of its beneficial effect to the alcohol it contains.

Dr. Robert N. Willson: I am by no means sorry to have my paper combated this evening. It would have been a source of regret to me had criticism been lacking, knowing as I do the uncompromising attitude of certain individuals with regard to the subject discussed. I am also afforded in this way an opportunity to reply to one or two misleading statements, far more "sweeping" and "irresponsible" than anything to be found in my paper. For instance, Dr. Hare ventured the assertion that I was guilty of ignorance of the first principles of cardiac physiology, on the basis of my having made a statement (as claimed by him) that alcohol or any other drug stimulates the heart by stimulating the vagus nerve. Where he was sojourning at the time I read the passage to which he inaccurately refers is a matter of some interest to me. What I actually did say, and which I now repeat, was that alcohol causes a stimulation of the cardiac action through its depressant action upon the vagus nerve. There is no one, I imagine, who is not familiar with the fact that the action of the vagus on the heart is inhibitory. Dr. Hare by his remark would appear to lay himself open to the suspicion of possible ignorance with respect to the action of the sympathetic nerve when the controlling influence of the vagus is set aside.

Again, I made no such statement as that alcohol produces arteriosclerosis. Indeed, I made absolutely the opposite assertion, namely, that there exists no final evidence that alcohol does produce arteriosclerosis. I did show that the combination of tobacco with alcohol often results in the production of arteriosclerosis. I also took pains to refer to the fact that the combined action of the two drugs gives a different result from that of alcohol alone. I well remember a discussion that took place some years

ago in Atlantic City when Richard Cabot read a paper on the innocence of alcohol with regard to the causation of arteriosclerosis, absolutely denying its complicity. Dr. Anders followed immediately with a satisfactory demonstration of the active influence of alcohol in producing arteriosclerosis. We have left behind the serious doubt of even that recent day. At the present moment the feeling is general that while alcohol certainly does contribute to the causation of arterial and myocardial disease, it does not produce by itself true arteriosclerosis, and for the very reason that Dr. Hare mentioned, namely, that alcohol dilates the arterioles by depressing the vasomotor system, and rather lowers than elevates the blood-pressure. Dr. Hare claims that the difference between the action of alcohol and tobacco lies in the fact that tobacco raises the diastolic and lowers the systolic blood-pressures, whereas alcohol lowers both in its secondary action. Dr. Hare is correct in his belief that the dominant action of alcohol is vasodilatation, after its first temporary splanchnic-constrictor influence. I called his attention to this fact in my paper. But he forgets the important fact that vasodilatation also characterizes tobacco, after its early vasoconstrictor action, and becomes its permanent influence. The evidence obtained from the action of both of these drugs is to the effect that vasoconstriction and the elevation of blood-pressure are not indispensable to the production of arterial disease.

I was sorry to hear Dr. Hare revert to the fallacy that alcohol is a food in any true sense of the word. I wish that he and all present might have heard Dr. A. E. Taylor's paper on this question presented a few evenings ago at the meeting already referred to by Dr. Hare. Dr. Taylor showed in a most conclusive manner that alcohol is never a food in the true sense; and that to call it such shows an entire ignorance of the readily available laboratory findings. Dr. Taylor's statement represents the consensus of intelligent medical opinion on the subject. To compare alcohol with sugar, for instance, is to ignore absolutely the fact that sugar is an actual food in the sense of supplying nutritive building material; while alcohol supplies at most a modicum of heat and energy when oxidized in the body. Moreover, alcohol tends to the destruction of protoplasm and to the production of disease, while sugar exercises neither influence.

With regard to Dr. Wood's remark, I will simply say that I mentioned three series of experiments which tend to confirm the experiments of Dixon. I did not attempt to mention all that Dixon had done, simply his conclusion, that the first action of alcohol is a stimulation of the heart. I also mentioned the fact that the experiments of Kohlmann verified Dixon's findings.

Finally, I avoided the tempting opportunity to stand on my own

authority. For every statement I made I gave ample clinical and laboratory evidence and the endorsement of men who are worthy of respect. If in the discussion tonight anyone has seemed to question the evidence which I have submitted, it will be well for him to remember that his questioning is of the accuracy of the statements of clinical and laboratory investigators known and trusted as such by the entire medical world.

SERUM STUDIES IN PREGNANCY

A STUDY OF THE SPECIFICITY OF FERMENTS IN PREGNANCY AND THE MECHANISM OF THE ABDERHALDEN REACTION (1) BY MEANS OF LOCAL SKIN REACTIONS; (2) BY PROTEOTOXIN PRODUCTION IN VITRO*

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Aside from the probable clinical value of the methods devised by Abderhalden in the serum diagnosis of pregnancy and various pathological conditions, such as malignancy, tuberculosis, lesions of the nervous system and ductless glands, most interest concerns the question of the specificity of the ferments or antibodies concerned and the mechanism of their action.

While Abderhalden and many of his pupils have claimed a high degree of specificity for the "protective ferments" and his pregnancy reaction, claiming from the beginning that errors of technic were largely responsible for the failure of others to obtain satisfactory results, the dialysis test as now conducted is not especially difficult and sufficient work has been done by other investigators who have followed Abderhalden's technic with great care and exactness to give warrant to the claim that other factors aside from those purely technical may be responsible for the divergent and non-specific results obtained.

As is well known, Abderhalden bases his theory concerning the

* Read May 5, 1915.

"protective ferments" upon the specific digestion of a substrate by specific ferments, claiming that these ferments are separate and distinct antibodies and not to be classed with the cytolytic amboceptors or cytolysins of Ehrlich.

That the substrate in the pregnancy test is a boiled tissue would seem to impair the specificity of the reaction and indeed certain physical factors as the mechanical state of division of the substrate and its facility for acting as an absorbent in a purely mechanical capacity likewise appear to be factors in the reaction on the basis of numerous investigations showing that loose areolar placental tissue is more frequently digested by normal sera and various pathological sera irrespective of pregnancy, whereas digestion of a firm and compact tissue as that of malignant tumors is much less constant. In this connection the work of de Waele[1] has a bearing, inasmuch as he found that any agent which would cause an alteration of the physical state of the serum globulins would cause an intense Abderhalden reaction, concluding that the reaction depended upon a globulinolysis having an origin in physical processes probably analogous to the precipitin reaction.

While immunological as well as chemical and physical reactions are more or less dependent upon quantitative factors, recent investigations by Flatow[2] and Herzfeld,[3] Plaut,[4] and others show that while specific results may be obtained by proper manipulation of the material, non-specific results in either a negative or positive reaction may be obtained with practically any serum, however well controlled, with the same material. These investigations are significant not so much because of quantitative factors alone as they are by reason of indicating that the pregnancy reaction is dependent upon the principles of mechanical absorption on the part of the substrate of something from the serum followed by a digestive process, rather than upon the simple digestion of a specific substrate by a specific ferment.

For this conception of the mechanism of the Abderhalden reaction the investigations of Jobling and Petersen[5] have been fundamental and of great interest and importance. They have shown that the digestive power of a serum is dependent upon non-specific proteolytic ferments or proteases normally present

and held in check by an antiferment, which, according to their work, is believed to reside in the unsaturated fatty acids of the serum. Upon removal of the antiferment by means of lipoidal solvents or saturation with various organic and inorganic substances as boiled tissue, iodine, starch, kaolin and the like, protease activity is released followed by digestion not of the so-called substrate but of the protein of the serum. Likewise Plaut,[6] Peiper,[7] Friedeman and Schonfield,[8] and Bronfenbrenner[9] have obtained positive Abderhalden reactions with guinea-pig and human sera not only with placental tissue but also with such inert substances as kaolin, starch, barium sulphate, chloroform, etc. These studies would therefore tend to show that the boiled placental tissue in Abderhalden's reaction is not digested but acts simply as an absorbent in a purely mechanical manner.

Furthermore, Heilner and Petri[10] and de Waele[11] found the ferments in the blood serum so quickly after the parenteral introduction of the protein, at intervals hardly sufficient for the elaboration of new and specific ferments as to support the theory that the ferments are preformed and that the substrate serves to activate these rather than bring about the production of new ferments.

Whether or not we regard Abderhalden's "protective ferments" in the serum of a pregnant animal as specific ferments or but an increase of normal and general proteolytic ferments, practically all investigators agree that they are to be found with regularity and in relatively large amounts in the serum during the later stages of pregnancy.

PART I

A STUDY OF THE SPECIFICITY OF FERMENTS IN PREGNANCY BY MEANS OF LOCAL SKIN REACTIONS

Granting, therefore, that mobilization of proteolytic ferments occurs during pregnancy, the object of our investigation was to determine: First, if extracts of placenta injected intracutaneously or applied to the abraded skin of pregnant women would be followed by the train of phenomena generally recognized as a local

anaphylactic or allergic reaction and ascribed to the action of a proteotoxin. According to a widely accepted theory the local and general phenomena of anaphylaxis are caused by an anaphylatoxin or protein poison, derived from the protein antigen or anaphylactogen through a process of protein cleavage or digestion by means of a specific lytic antibody and a complement. Our object was to determine if this cleavage could be detected *in vivo* in the form of a local anaphylactic reaction. Second, if such a reaction occurs whether it is due to specific or general ferments and under what circumstances it would occur.

The question of the relation of anaphylaxis to labor was studied experimentally by Sauerbruch and Heyde[12] who found upon attaching together in parobiosis pregnant and non-pregnant rats that all was well until the onset of labor, when the non-gravid animals developed convulsive seizures, suggestive of uremia, and not infrequently died. As a result of these observations Heide[13] took up the subject and injected placental serum intravenously into twenty-one pregnant women at term or during labor. In thirteen cases labor was hastened, or weak pains and uterine contractions intensified; in eight cases the results were negative. In the following year Rongy[14] reported even better results with nineteen cases, using the technic of Heide. From the fact that the mental factor attending an intravenous injection itself may considerably influence a woman in labor or at term regardless of what is injected, one of us, Kolmer,[15] studied the subject experimentally in pregnant guinea-pigs, as intravenous injections may be given these animals with very little handling and trauma and the mental factor largely eliminated. After injecting pregnant guinea-pigs at or very near term with pig placental serum, pig maternal serum and human maternal and placental serum the results were regarded on the whole as negative, although a few animals did fall into labor shortly after the injections. The intravenous injections of a placental extract (guinea-pig) was followed by labor in two of the three animals used. With the assistance of Drs. Anspach and Narr, human placental serum was injected subcutaneously into eight pregnant women near term or in labor in doses varying from 10 to 30 c.c. with practically

no effect, either upon the uterus or in general that could be ascribed to the serum.

Fromme[16] used fetal serum applied to the abraded skin or injected subcutaneously in pregnant women with negative results. With fresh ox serum, however, he observed a number of reactions consisting of an edematous, red and tender swelling at the site of injection. These negative results with fetal serum led him to believe that the mother is not sensitized by fetal products during the period of normal gestation.

Esch[17] observed negative results with fetal serum. Later Esch[18] injected pregnant women intra- and subcutaneously with horse serum and placental extract with negative results, and also showed that the urine of parturient women does not become highly toxic as does the urine of animals during anaphylactic shock. He advanced these results against Heide's theory that labor is a form of anaphylactic reaction due to the sensitization by the proteids of the fetus or placenta.

Lately Engelhorn and Wintz[19] have reported positive results in a small series of pregnant women following the application of *placentin* to an area of abraded skin. They gave no account of the preparation of their *placentin* except to state that the process was intricate. Esch[20] used expressed whole placental juice as well as the globulin and albumin fractions in the same manner with questionable results. De Jong[21] prepared a 10 per cent. watery suspension of dried hog placenta and injected 0.1 c.c. intracutaneously into a series of animals. In both pregnant and non-pregnant animals a slight infiltration of the tissues followed. He then dropped small amounts of the same material upon the conjunctiva of the animals with indefinite results. Further work led him to believe that the maternal antigen as he called it was either non-irritating or not seized upon and digested and concluded that the method had no practical value.

Falls and Bartlett[22] used aqueous, saline, and acid extracts, and glycerin emulsions of placenta in a series of thirty-three cases. These preparations were used intra- and percutaneously; and in both pregnant and non-pregnant persons caused a certain degree of reaction. The difference was not considered sufficient to be of

value in diagnosis, and the absence of a pronounced general reaction was taken as evidence that the pregnant woman was not specifically sensitized to placental proteids.

ORIGINAL INVESTIGATIONS

Placental Extracts (Placentins). We have prepared a number of placental extracts of fresh full-term placentas in several ways, our object being to disrupt the cells and secure the cellular tissue as finely divided and unchanged as possible. To this end placental tissue was washed, thoroughly ground, subjected to high pressure and the juice so obtained concentrated and preserved. Glycerin extracts were also prepared and used for cutaneous inoculation. The exact technic of preparing the several extracts will be given later.

Control Extracts. Early in this investigation we were impressed with the necessity of controlling the work not only by using the *placentins* in non-pregnant persons but also by using control extracts prepared from another tissue in pregnant women. To this end a salt solution was prepared by evaporating to one-half volume 200 c.c. of normal salt solution containing 0.05 per cent. glycerin and 0.25 per cent. tricresol and used in controlling *placentin* No. 1 which was prepared by concentrating placental juice after the same manner. We also prepared and used extracts of beef kidney and human male and female kidney in exactly the same manner as the several *placentins.*

Patients. Our patients may be divided into three groups as follows:

(*a*) Pregnant and puerperal women.

(*b*) Non-pregnant women, who have been pregnant one or more times.

(*c*) Controls, women who claim never to have been pregnant, and men.

Methods of Administration and Dosage. The *placentins* and *nephrins* were employed diluted and undiluted, mostly in doses of 0.05 c.c. and never over 0.1 c.c., in order to reduce trauma to a minimum. All injections were given with a fine (No. 26) gauge needle.

TABLE No. 1.—Skin Reactions in Pregnancy and the Puerperium following the Intracutaneous Injection of 0.05 c.c. of Placentin No. 1 (undiluted), and of 0.05 c.c. of Control Fluid.

No.	Race.	Para.	History.	Placentin reaction.			Control fluid reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
1	White	1	At term	4.5 x 4.5	Marked*	Slight**	2 x 1.5	Slight	Slight.
2	Colored	0	At term	Faint	..	..	—***	Slight	Slight.
3	White	1	21 days post-abortion	1 x 1	Slight	..	Faint	..	—
4	White	1	4 months pregnant	5.5 x 4.5	Moderate	..	3.5 x 3	..	—
5	White	3	7 days post-abortion	3 x 2	Slight	..	Faint	..	—
6	Colored	4	10 days post-partum	5 x 4.5	Moderate	..	Faint	..	—
7	White	2	13 days post-partum	2.5 x 4	..	..	—	..	—
8	White	1	14 days post-partum	3 x 3	Slight	..	—	..	—
9	White	1	8 hours post-partum	8 x 4.5	Moderate	..	Faint	..	Slight.
10	White	1	8 hours post-partum	4 x 5	..	..	—	Slight	—
11	Colored	1	23 days post-partum	—	Slight	—	—	—	—
12	White	1	4 days post-partum	—	..	—	—	—	—
13	White	1	12 days post-partum	4 x 3	Moderate	Slight	Faint	Slight	—
14	White	1	At term	2 x 3	Slight	..	—	—	—
15	White	2	At term	4 x 3.5	Moderate	..	—	—	—
16	Colored	1	8 months pregnant	—	Slight	..	—	—	—
17	White	1	1 month pregnant (doubtful)	2 x 2	..	..	—	—	—
18	Colored	1	At term	3.5 x 3	Moderate	..	—	—	—
19	White	2	6 months pregnant	Faint	Slight	—	—	—	—
20	Colored	0	At term	—	Slight	—	—	—	—
21	Colored	1	6 months pregnant	—	Slight	—	—	—	—
22	Colored	1	7 months pregnant	—	Slight	—	—	—	—
23	White	5	6 months pregnant	4 x 3	Moderate	Slight	Faint	Slight	—
24	Colored	0	8 months pregnant	—	Slight	Slight	—	—	—
25	White	0	At term	3 x 3	Moderate	Slight	—	—	—
26	Colored	0	At term	Faint	Slight	—	0****	0	0
27	Colored	3	At term	—	Slight	—	0	0	0
28	White	2	At term	4 x 4.5	Slight	Slight	0	0	0
29	White	0	At term	3 x 3	Slight	Slight	0	0	0
30	White	0	7 months pregnant	Faint	Slight	—	0	0	0
31	Colored	1	At term	Faint	Marked	Slight	0	0	0
32	White	0	6 months pregnant	4 x 2.5	Marked	Marked	0	0	0
33	White	1	1 month pregnant	—	—	—	0	0	0
34	Colored	2	10 days post-partum	2 x 2	Slight	Slight	0	0	0
35	White	7	3 days post-partum	3.5 x 3	Slight	Slight	0	0	0
36	Colored	1	7 days post-partum	—	—	—	0	0	0
37	White	3	21 days post-partum	—	—	—	0	0	0
38	White	0	Abortion at 3 months	—	—	—	0	0	0

39	White	3	Last child 7 years ago	1 x 2	Slight	—	0	0	0
40	White	4	At term	3 x 3	Moderate	—	0	0	0
41	White	0	At term	3.5 x 2.5	Moderate	Slight	0	0	0
42	White	1	At term	2 x 3.5	Moderate	Slight	0	0	0
43	White	0	At term	4.5 x 3	Slight	Slight	0	0	0
44	White	0	At term	3 x 3	Slight	—	0	0	0
45	White	2	14 days post-partum	2.5 x 1.5	Slight	Slight	0	0	0
46	White	4	14 days post-partum	3.5 x 2	Moderate	..	0	0	0
47	White	11	14 days post-partum	4 x 5	Marked	Moderate	0	0	0
48	White	1	10 days post-partum	Faint	Slight	—	0	0	0
49	White	4	11 days post-partum	4 x 3	Marked	Slight	0	0	0
50	White	3	At term	3.5 x 3	..	..	0	0	0
51	White	2	3 days post-partum	Faint	—	—	0	0	0
52	White	3	24 days post-partum	3 x 2	Moderate	Slight	0	0	0
53	White	8	16 days post-partum	—	—	—	0	0	0
54	White	1	28 days post-partum	Faint	—	—	0	0	0
55	White	1	4 days post-partum	6 x 2	Marked	Moderate	0	0	0
56	White	0	At term	2.5 x 3	Slight	Slight	0	0	0
57	Colored	0	At term	—	..	..	0	0	0
58	Colored	0	At term	—	..	..	0	0	0
59	White	0	8 months pregnant	1 x 1	..	—	0	0	0
60	White	0	At term	3.5 x 4	Moderate	—	0	0	0
61	White	0	At term	3 x 4	Slight	Slight	0	0	0
62	White	2	20 days post-partum	1 x 1.5	..	—	0	0	0
63	White	1	10 days post-partum	4 x 4	Marked	Slight	0	0	0
64	White	2	6 days post-partum	3 x 4	Moderate	Slight	0	0	0
65	White	1	4 days post-partum	2 x 2	Slight	Slight	0	0	0
66	White	0	At term	1 x 1	Slight	—	0	0	0
67	Colored	0	At term	—	Slight	Slight	0	0	0
68	Colored	1	At term	—	Slight	—	0	0	0
69	Colored	0	At term	—	..	Slight	0	0	0
70	White	0	At term	—	..	..	0	0	0
71	White	1	9 days post-partum	—	—	—	0	0	0
72	White	2	8 days post-partum	6 x 4.5	Slight	Slight	0	0	0
73	Colored	1	6 days post-partum	—	Slight	—	0	0	0
74	Colored	0	7 months pregnant	2 x 2	..	Slight	0	0	0
75	Colored	0	At term	—	..	..	0	0	0
76	White	1	21 days post-partum	Faint	—	—	0	0	0
77	Colored	1	7 months pregnant	—	Slight	Slight	0	0	0
78	Colored	1	14 days post-partum	—	—	—	0	0	0
79	Colored	1	14 days post-partum	—	Slight	—	0	0	0
80	Colored	1	28 days post-partum	1.5 x 1.5	..	—	0	0	0

* Degree of infiltration as determined by palpation, was recorded only where it was greater than could be expected from trauma alone.

** Degree of pain according to patient's statement at time lesion was palpated.

*** — = Negative.

**** 0 = Not tested.

TABLE No. 2.—Skin Reactions in Parous and Supposedly Nulliparous Women following Intracutaneous Injection of 0.05 c.c. of Placenta No. 1 (undiluted).

No.	Race.	Para.	History.	Placentin reaction.			Control fluid reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
81	White	0	Appendicitis	4 x 3	Slight	Slight	—	Slight	—
82	White	1	Last child 4 years ago	3 x 1.5	Moderate	Slight	—	—	—
83	White	1	Last child 10 weeks ago	3 x 3	Moderate	Slight	—	—	—
84	White	1	Last child 3 years ago	3 x 3	Slight	Slight	—	—	—
85	White	2	Both miscarriages; last 1 year ago	3 x 2	Slight	Slight	—	—	—
86	White	1	Miscarriage 6 months ago	—	Slight	—	—	—	—
87	White	2	Last child 12 years ago; gonorrhea	4 x 3	Slight	Slight	—	—	—
88	White	0	Gonorrhea	—	Slight	—	—	—	—
89	White	0	Tuberculosis and syphilis	4 x 2.5	Slight	Slight	—	—	—
90	White	0	Gonorrhea	—	—	—	—	—	—
91	White	0	Gonorrhea	2 x 3	Slight	Slight	—	—	—
92	White	0	Gonorrhea	—	—	—	—	—	—
93	Colored	1	Last child 13 months ago; gonorrhea	2 x 2	Slight	Slight	Faint	Slight	—
94	White	0	Gonorrhea	2 x 2.5	Slight	—	—	—	—
95	White	0	Gonorrhea	4 x 3.5	Moderate	Moderate	Faint	Slight	Slight.
96	White	0	Syphilis	3.5 x 3	Slight	Slight	—	—	—
97	White	0	Gonorrhea	—	—	—	—	—	—
98	White	0	Gonorrhea	—	—	—	—	—	—
99	Colored	0	Gonorrhea	—	—	—	—	—	—
100	White	1	Last child 6 months ago	—	—	—	—	—	—
101	White	0	Ovarian cyst	—	—	—	—	—	—

Glycerin and watery extracts were also employed after the manner of applying the cutaneous tuberculin test.

Reactions. Local reactions characterized by erythema, edematous infiltration and pain were frequently observed not only with the *placentins*, but also, as will be pointed out later with the controls. The reactions were generally recorded twenty-four hours after the inoculation. With few exceptions the patients did not complain of pain in the axilla and in no instance were general reactions observed, although one of us experienced slight headache and malaise after intracutaneous injection of the *placentins* and *nephrins*. In colored persons the erythema could be seen, but not accurately measured. In many of these persons we were able to detect infiltration without noting erythema.

RESULTS WITH PLACENTIN NO. 1

Preparation. Recently delivered placentas were trimmed of the cords and membranes, cut into small pieces, washed in warm water and passed through a meat grinder. The minced tissue was then washed for twenty-four hours in running water until quite free of blood, and as white as possible. After squeezing out the excess of water the tissue was ground in mortars with sterile powdered quartz and the finely divided pulpy material pressed at 200 pounds in a Buchner hydraulic press. The clear yellowish and opalescent fluid so obtained was centrifuged at high speed to remove particles of quartz, filtered through hard filter paper; measured and 0.5 per cent. glycerin and 0.25 per cent. tricresol added as a preservative. The juice was then concentrated to one-half volume at 40° C., during which a light precipitate was thrown down. The clear supernatant fluid was pipetted off, filtered through sterile paper and a sterile Berkefeld filter, its sterility tested by culture, and injected subcutaneously in rabbits. After having been proved sterile, this undiluted *placentin* was injected intracutaneously in doses of 0.05 c.c.; also diluted 1 to 10 in the same amount.

The results observed with this *placentin* and the control fluid are shown in Tables 1 and 2.

TABLE No. 3.—Placentin No. 1.—Skin Reactions in Pregnancy and the Puerperium following the Intracutaneous Injection of 0.05 c.c. of Placentin No. 1 (diluted 1 to 10); also Results with 0.05 c.c. Nephrin (diluted 1 to 10).

No.	Race.	Para.	History.	Placentin reaction.			Nephrin reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
132	White	1	3 days post-abortion	—	—	—	—	—	—
133	White	11	4 days post-partum	Slight	—	—	—	—	—
134	White	4	3 days post-partum	3 x 2.5	Slight	Slight	Faint	Slight	—
135	White	1	21 days post-partum	2 x 2	Moderate	Slight	—	—	—
136	White	2	4 days post-partum	1 x 1	Slight	—	—	—	—
137	Colored	3	At term	Slight	Slight	—	—	—	—
138	Colored	2	5 days post-partum	—	—	—	—	—	—
139	White	7	14 days post-partum	2 x 2	Slight	Slight	Faint	—	—
140	White	0	At term	1.5 x 1.5	Slight	Slight	—	—	—
141	White	1	10 days post-partum	Faint	—	—	—	—	—

TABLE No. 4.—Skin Reactions in Parous and Supposedly Nulliparous Women following Intracutaneous Injections of 0.05 c.c. of Placentin No. 1 (diluted 1 to 10) and 0.05 c.c. Nephrin (diluted 1 to 10).

No.	Race.	Para.	History.	Placentin reaction.			Nephrin reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
142	White	10	Last child 10 years ago	3 x 2.5	Slight	Slight	—	—	—
143	White	2	Last child 6 years ago	1 x 1	Slight	—	—	—	—
144	White	10	Last child 18 years ago	—	—	—	—	—	—
145	White	0	Appendicitis	2 x 2	Slight	Slight	—	—	—
146	White	0	Normal	—	—	—	—	—	—
147	White	1	Last child 2 years ago	—	—	—	—	—	—
148	White	4	Last child 3 years ago	—	Slight	—	—	—	—
149	White	9	Last child 15 years ago	1 x 1	Slight	—	—	—	—
150	White	0	Normal	Faint	—	—	—	—	—
151	White	0	Normal	2 x 2	Slight	Slight	—	—	—

1. Accepting infiltration of the tissues as the most constant sign of a reaction, since erythema may not readily be appreciated in colored women, it was found that 87 per cent. of eighty women who were pregnant or recently delivered reacted positively with this *placentin*. The reactions were usually well defined and easily read.

2. The significance of these reactions is lessened by the fact that 52 per cent. of these women tested with a control fluid prepared in the same manner as the *placentin* yielded weak reactions.

3. Of twenty-one women who were either delivered six months or more prior to these tests or who claim never to have been pregnant, fourteen, or 66 per cent., reacted positively with the *placentin* and three, or 14 per cent., with the control fluid. It may be stated that eleven of these women who claim never to have been pregnant were in the venereal wards of the Philadelphia General Hospital with syphilis or gonorrheal urethritis or vaginitis and had been exposed to impregnation.

4. In general the reactions with the control fluid occurred in those women who reacted with the *placentin*.

5. This *placentin* and the control fluid were also injected in the same dosage and manner in thirty men (102–132). In six, or 20 per cent., a slight area of erythema (0.5 to 1 cm.) and infiltration followed.

6. We are inclined to believe that the glycerin in our extract acted as an irritant, this action being especially well marked in pregnant women whose skins were hypersensitive.

On the basis that many of these reactions were caused by an irritant action of the glycerin and tricresol contained in the *placentin* and control fluids, intensified by a hypersensitiveness of the skin in pregnancy, another series of persons were tested with these fluids diluted 1 to 10 with normal salt solution. In this dilution the control fluid did not give any reactions at all, and in order to control the *placentins* with other tissue extracts two kidney extracts or *nephrins* were prepared of beef and human male kidney in a manner as similar to the *placentin* as we were able to prepare them.

The employment of these extracts yielded results as shown in Tables 3 and 4.

1. With the diluted *placentin* 80 per cent. of the women tested who were either pregnant or recently delivered reacted positively. As a general rule, the reactions were weaker than those obtained with the undiluted *placentin.*

2. Of six women who had borne children three, or 50 per cent., reacted positively.

3. Of four women who claim never to have been pregnant three reacted positively.

4. Two of the ten women who were pregnant or recently delivered reacted slightly with an extract of human male kidney.

RESULTS WITH PLACENTIN NO. 4

In order to further eliminate the question of traumatic reactions with extracts preserved with glycerin and tricresol, another *placentin* was prepared as follows: Placental juice was obtained in exactly the same manner as described in the preparation of *placentin* No. 1, filtered through paper and evaporated to one-half volume at 40° C., preserved with chloroform vapor. The supernatant fluid was then filtered four times through hard filter paper to remove the chloroform and then filtered once through a sterile Berkefeld filter. The resulting clear yellowish fluid was preserved with 0.25 per cent. tricresol and injected intracutaneously in doses of 0.05 c.c. Glycerin was not added and the minimum quantity of tricresol is in itself devoid of irritant action when injected intracutaneously.

An extract of human female kidney (*nephrin*) was prepared at the same time and in the same manner and injected in a similar dose.

(For results obtained see Table 5.)

1. Of the forty women who were either pregnant or recently delivered at the time of the tests, sixteen, or 40 per cent., reacted positively with the *placentin.* Thirteen of these women were also tested at the same time with the extract of human female kidney and five, or 38 per cent., gave a positive reaction. In general, these reactions were weaker than those observed with *placentin* No. 1 due, we believe, to the absence of glycerin.

2. Of twenty-two women who had been pregnant one or more times prior to these tests, three, or about 14 per cent., reacted positively and nineteen, or 86 per cent., reacted negatively. Seventeen of these women were also tested at the same time with the *nephrin* and seven, or 42 per cent., reacted positively and ten, or 49 per cent., reacted negatively.

3. Of three women who claim never to have been pregnant, one, a colored woman of thirty-eight years, reacted positively with both the *placentin* and *nephrin*.

4. Eight men (217–224) were also injected with this *placentin* and *nephrin;* all of these reacted negatively with the *placentin* and three showed a slight erythema and infiltration with the *nephrin*. This shows that the nephrin was probably more irritant than the *placentin* and tends to explain the higher percentage of reactions among women who were not pregnant at the time these tests were made.

5. As will be noted, the percentage of reactions among pregnant and recently delivered women with this *placentin* was lower than that observed with *placentin* No. 1. Whether this difference was due to the absence of an irritant action due to the glycerin or whether the glycerin served to extract a principle in the first *placentin* which was absent in this one we are unable to state. Since, however, the first *placentin* when diluted 1 to 10 gave a higher percentage of reactions (80 per cent.), it is probable that the glycerin serves to extract an antigenic principle.

RESULTS WITH PLACENTIN NO. 2

Preparation.. While evaporating to one-half volume the placental juice prepared as described in the preparation of *placentin* No. 1, a finely divided precipitate was deposited on the sides and bottom of the dish, composed of material so finely divided as to stay in suspension after centrifuging and filtering the juice through hard paper, but which was thrown down as a result of evaporation and concentration.

TABLE No. 5.—Placentin No. 4.—Skin Reactions in Pregnant, Parous and Supposedly Nulliparous Women following Intracutaneous Injections of Placentin No. 4 and Human Female Kidney Extract (Nephrin).

No.	Race.	Para.	History.	Placentin reaction.			Nephrin reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
152	Colored	1	At term	—	—	—	—	—	—
153	Colored	0	At term	—	Slight	—	—	—	—
154	White	3	28 days post-partum	—	—	—	—	Slight	—
155	White	1	15 days post-partum	—	—	—	—	—	—
156	Colored	1	30 days post-abortion	—	—	—	—	—	—
157	White	2	Last child 3 years ago	—	—	—	Faint	—	—
158	White	3	Last child 2 years ago	Faint	Slight	—	Faint	—	—
159	White	2	Last child 14 years ago	—	—	—	—	—	—
160	White	6	Last child 15 years ago	—	—	—	—	—	—
161	White	4	Last child 9 years ago	—	—	—	—	—	—
162	White	9	28 days post-partum	—	—	—	—	—	—
163	White	1	10 days post-partum	2 x 2.5	Slight	Slight	2 x 3	Slight	Slight.
164	White	1	12 hours post-partum	Faint	Slight	—	1 x 1.5	Slight	—
165	White	2	Last child 4 months ago	—	—	—	—	—	—
166	White	1	Last child 16 years ago	—	—	—	2 x 2	Slight	—
167	White	3	10 days post-partum	—	—	—	2 x 2	Slight	—
168	Colored	1	24 days post-partum	—	—	—	—	—	—
169	Colored	2	9 days post-partum	—	—	—	—	—	—
170	White	1	Last child 16 years ago	—	—	—	Faint	Slight	—
171	White	5	5 days post-partum	—	—	—	—	—	—
172	White	1	Last child 1 year ago	—	—	—	—	—	—
173	White	4	Last child 16 years ago	—	—	—	—	—	—
174	Colored	0	Nullipara	Faint	Slight	—	Faint	Slight	—
175	White	5	Last child 17 years ago	2 x 2	Slight	—	2 x 2	Slight	—
176	White	1	Last child 14 years ago	—	—	—	—	—	—
177	White	0	Nullipara	—	—	—	—	—	—

| | | |

Evaporation was continued until the residue was a thick pulpy mass and 2.5 grams were suspended in 100 c.c. of sterile normal salt solution. The resulting suspension was probably composed of very finely divided particles of placental tissue; when completely dried the material contained 5.39 per cent. nitrogen.*

This *placentin* was injected intracutaneously in a dose of 0.05 c.c. and the effects noted after twenty-four and forty-eight hours.

As a control a similar suspension was made of the residue obtained in the preparation of a *nephrin* from human male kidney; this was injected intracutaneously in a dose of 0.05 c.c.

(For the results following the use of these preparations See Tables 6 and 7.)

1. Of forty pregnant or recently delivered women, twenty-two, or 55 per cent., reacted positively; in this same group the *nephrin* caused a positive reaction in 20 per cent.

2. Of nine women who had been pregnant one or more times prior to the tests, five, or 55 per cent., reacted positively with the *placentin*, and three, or 33 per cent., reacted positively with the *nephrin*.

3. In all instances the positive *nephrin* reactions occurred among women reacting positively with the *placentin*.

4. Two women, claiming never to have been pregnant, reacted negatively with both the *placentin* and *nephrin*.

5. Of twenty men (277 to 296) tested with *placentin* No. 2, four, or 20 per cent., showed a small area of erythema and very slight infiltration twenty-four hours later. All except three of these men were suffering with gonorrhea or syphilis.

RESULTS WITH PLACENTINS NOS. 3, 5, 6

Glycerin Extracts. These glycerin extracts of placental tissue were prepared and tested by cutaneous inoculation after removal of a small area of skin with a von Pirquet borer. A control scarification was made on the same arm, the *placentin* being applied to the lower abrasion.

* For this analysis we are indebted to Dr. A. J. Ringer, of the Laboratory of Physiological Chemistry.

Placentin Reaction.

Reaction twenty-four hours after the intracutaneous injection of 0.05 c.c. of placentin, No. 2. Patient delivered of a full-term child four hours before the injection was made.

The reactions were recorded as negative when the *placentin* and control sites were equal in appearance and diameter; when the *placentin* site showed an areola of erythema this was measured in millimeters.

Preparation. *Placentin* No. 3. This was prepared by rubbing up in a mortar equal parts of *placentin* No. 2 (residue from placental juice) and neutral glycerin. It constituted, therefore, a suspension of No. 2 in glycerin rather than a true glycerin extract.

Placentin No. 5. To 100 grams of fresh, finely minced and washed placental tissue 75 c.c. glycerin and 225 c.c. of normal salt solution were added and the mixture incubated at 37° C. for two weeks. At the end of this time the fluid portion was filtered and evaporated to one-half volume, the resulting fluid now being a 50 per cent. glycerin extract.

Placentin No. 6. To 190 c.c. of placental juice to 10 c.c. of glycerin were added and the mixture incubated at 37° C. for two weeks. At the end of this time the fluid was filtered through paper and evaporated at 40° C. to 20 c.c; the *placentin* was now a 50 per cent. glycerin extract.

These extracts were used with the following results:

1. *Placentin* No. 3 was tested upon forty-five persons (297 to 341), chiefly women who were pregnant or recently delivered. All reacted negatively except two, (*a*) a woman at term whose *placentin* reaction measured 4 mm. in diameter more than the control reaction, (*b*) a woman delivered of a full-term child twenty days previously whose *placentin* reaction measured 6 mm. in diameter more than the control site.

2. *Placentin* No. 5 was tested upon twenty-two persons (342 to 363), (*a*) of eighteen pregnant or recently delivered women, nine or 50 per cent. reacted positively showing an areola about the *placentin* site measuring from 4 to 16 mm. in diameter more than the control site, (*b*) two women who had borne children several years previously reacted negatively, (*c*) two women, claiming never to have been pregnant, reacted negatively. This *placentin*, a true glycerin extract of placental cells, yielded the largest number of positive reactions.

TABLE NO. 6.—Placentin No. 2.—Skin Reactions in Pregnant and Recently Delivered Women following the Intracutaneous Injection of 0.05 c.c. of Placentin No. 2 and Human Male Nephrin.

No.	Race.	Para.	History.	Placentin reaction.			Nephrin reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
225	White	6	3 days post-partum	2 x 2.5	Slight	—	Faint	Slight	Slight.
226	White	1	4 days post-partum	1.5 x 1.5	Slight	Slight	—	—	—
227	White	1	5 days post-partum	.75 x 1	Slight	—	—	—	—
228	White	8	2 days post-partum	Faint	Moderate	Slight	—	—	—
229	White	4	At term	2 x 2	Slight	Slight	Faint	—	—
230	White	2	4 days post-partum	—	—	—	—	—	—
231	Colored	1	10 days post-partum	2 x 2	Slight	Slight	—	—	—
232	Colored	0	At term	—	—	—	—	—	—
233	Colored	3	At term	—	—	—	—	—	—
234	White	2	At term	3 x 3	Slight	Slight	—	—	—
235	White	0	At term	3 x 3	Marked	Slight	0	0	0
236	White	0	7 months pregnant	Faint	Slight	—	0	0	0
237	Colored	1	At term	—	Slight	—	0	0	0
238	White	0	6 months pregnant	2 x 1.5	Slight	Slight	0	0	0
239	White	1	1 month pregnant	—	—	—	0	0	0
240	Colored	2	10 days post-partum	Faint	—	—	0	0	0
241	White	7	3 days post-partum	—	—	—	0	0	0
242	Colored	1	7 days post-partum	—	—	—	0	0	0
243	White	3	21 days post-partum	Faint	—	—	0	0	0
244	White	3	10 days post-partum	Faint	Slight	—	0	0	0
245	White	1	6 days post-partum	1 x 1.5	Slight	—	0	0	0
246	White	1	21 days post-partum	—	—	—	0	0	0
247	White	1	At term	3 x 2.5	Slight	Slight	0	0	0
248	White	2	10 days post-partum	—	Slight	—	0	0	0
249	White	1	12 days post-partum	1.5 x 2	Slight	—	0	0	0
250	White	3	3 days post-partum	—	—	—	0	0	0
251	White	2	14 days post-partum	3 x 3	Slight	—	0	0	0
252	White	1	4 days post-partum	—	—	—	0	0	0
253	White	1	9 days post-partum	4 x 3	Moderate	Slight	0	0	0

254	White	2	9 days post-partum	—	—	—	0	0	0
255	White	5	2 days post-partum	2.5 x 3	Slight	Slight	0	0	0
256	White	2	4 days post-partum	—	Slight	—	0	0	0
257	Colored	1	28 days post-partum	—	—	—	0	0	0
258	White	2	9 days post-partum	.7 x 1.0	—	—	0	0	0
259	White	1	2 days post-partum	—	—	—	0	0	0
260	Colored	5	.....	2 x 2.5	Slight	—	0	0	0
261	Colored	0	7 months pregnant	—	—	—	0	0	0
262	Colored	1	14 days post-partum	—	—	—	0	0	0
263	Colored	1	10 days post-partum	—	—	—	0	0	0
264	White	1	3 days post-partum	—	—	—	0	0	0

TABLE No. 7.—Placentin No. 2.—Skin Reactions in Parous and Supposedly Nulliparous Women following Intracutaneous Injection of 0.05 c.c. of Placentin No. 2.

No.	Race.	Para.	History.	Placenta reaction.			Nephrin reaction.		
				Erythema, cm.	Infiltration.	Pain.	Erythema, cm.	Infiltration.	Pain.
265	White	0	Appendicitis	—	—	—	—	—	—
266	White	2	Last child 7 years ago	3 x 2.5	Slight	Slight	1 x 1.5	Slight	Slight.
267	White	2	Last child 6 years ago	1 x 1	Slight	—	—	Slight	—
268	White	3	Last child 7 years ago	—	—	—	—	—	—
269	White	4	Last child 10 years ago	1 x 1.5	Slight	—	—	—	—
270	White	4	Last child 2 years ago	—	—	—	—	—	—
271	White	3	Last child 15 years ago	—	—	—	—	—	—
272	White	5	Last child 11 years ago	1 x 1	Slight	—	—	Slight	—
273	White	5	Last child 7 years ago	2 x 2	Slight	—	—	—	—
274	....	0	Fibroid uterus	—	—	—	—	—	—
275	....	5	Last child 15 years ago	—	—	—	—	—	—
276	White	2	Cancer of cervix	—	—	—	—	—	—

3. *Placentin* No. 6 was tested upon twelve persons (364 to 375), mostly pregnant and recently delivered women; all reacted negatively except three, these being women at term whose *placentin* reaction measured 3, 5, and 7 mm. in diameter more than their respective control reactions.

4. *Placentin* No. 1 was also tried locally with five women at term (376 to 380) all reacting negatively.

SUMMARY OF PART I

1. A *placentin* No. 1 prepared by concentration of expressed placental juice, preserved with 1 per cent. glycerin and 0.5 per cent. tricresol and injected intracutaneously yielded skin reactions characterized by erythema, infiltration and pain in 87 per cent. of pregnant and recently delivered women, and in 66 per cent. of women who had borne children, but who were not pregnant at the time these tests were made. This extract also caused 20 per cent. of the men tested to react slightly.

2. When diluted 1 to 10 with normal salt solution this extract yielded 80 per cent. positive reactions among pregnant or recently delivered women, and 50 per cent. positive among women who had borne children.

3. A *placentin* (No. 4) prepared in the same manner as the first extract except that glycerin was not used in its preparation or preservation, yielded 40 per cent. positive reactions among pregnant or recently delivered women, and 14 per cent. positive reactions among women who had borne children. It is probable that glycerin itself acts as an irritant, especially in the hypersensitive skin of pregnant women.

4. A *placentin* (No. 2) prepared from the residue resulting from the concentration of expressed placental juice yielded 55 per cent. positive reactions among women who were pregnant or recently delivered. This *placentin* produced slightly positive results in 20 per cent. of the men tested.

5. A glycerin extract (*placentin* No. 5) upon cutaneous inoculation yielded 50 per cent. positive reactions among pregnant and

recently delivered women. Of several multiparous and nulliparous women tested, all reacted negatively.

6. Extracts of human male and female kidney (*nephrins*) prepared in the same manner as the *placentins* produced a number of positive reactions among pregnant, puerperal, multiparous and nulliparous women. The most marked reactions were observed with the extract of human female kidney.

Part II

A STUDY OF THE SPECIFICITY OF THE FERMENTS IN PREGNANCY AND THE MECHANISM OF THE ABDERHALDEN REACTION BY PROTEOTOXIN PRODUCTION IN VITRO

These results induced us to continue the work and study the specificity of the ferments and the mechanism of this action along a similar line, inasmuch as most of the previous investigations in this subject were conducted after the dialysis method of Abderhalden, the occurrence and degree of digestion being determined by the ninhydrin test with the dialyzable products of protein digestion. Jobling and Peterson, however, have used another technique consisting in the removal of the antiferment by lipoidal solvents or absorption by various organic and inorganic substances and studying the digestive activity and specificity of the proteolytic ferments by chemical methods.

As we had reason to believe in our previous investigation that proteotoxins were produced *in vivo* and that these were responsible for the local skin reactions we have continued our work by bringing about proteotoxin production *in vitro* and testing for its presence in sera by means of local skin reactions and general intoxication following respectively the intracutaneous and intravenous injection of the material. By these methods the results of which are given in this communication we hope to bring forward additional information regarding the specificity of the ferments and the mechanism of their action.

This method of study is based upon the work of several investigators as Friedman,[23] who produced a protein poison by digesting ox corpuscles with immune and normal rabbit serum; by Weichardt[24] as the result of the digestion of placental protein with rabbit immune serum and by Friedberger,[25] who digested a serum precipitate with normal guinea-pig serum, the results of these investigations being similar to those of Vaughan and Wheeler,[26] who several years previously obtained toxic substances capable of producing symptoms and lesions analogous to acute anaphylaxis by splitting proteids of various origin with alcoholic sodium hydroxide solution. Subsequent studies by Priedberger and his collaborators,[27] [28] by Dold and Aoki[29] and others have shown that similar protein poisons could be obtained by digesting various microörganisms with fresh normal guinea-pig serum, all of these investigators regarding the protein poison as derived from the protein antigen by means of a process of digestion.

As the effects of these protein poisons produced *in vitro* in the living animal were similar to the symptoms and lesions observed in acute anaphylaxis, Friedberger has called them anaphylatoxins and this term has come into such general use that it is applied to any poisonous protein substance able to produce in normal animals the phenomena of anaphylaxis. At present however, we prefer to call this substance proteotoxin.

Briefly the objects of this investigation were as follows:

1. To determine by means of intracutaneous and intravenous injections of the material if proteotoxins are produced during the Abderhalden reaction.

2. To study the specificity of the ferments in pregnancy by the same methods.

3. To study the mechanism of the reaction and particularly the source of the protein matrix.

4. To study the relation of complement to the proteolytic ferments of pregnancy.

I. Proteotoxin Production in a Mixture of Pregnancy Serum and Placental Tissue

Technique. Sera were secured from pregnant women at or near term under strict aseptic precautions and from four to five hours after a meal. These sera were then thoroughly centrifugalized to render them corpuscle free and used within three hours after bleeding. Placental tissue was prepared as directed by Abderhalden. With each serum an Abderhalden reaction was conducted in the usual manner with tested and satisfactory shells in order to compare the effects of proteotoxin *in vivo* with the occurrence and degree of the ninhydrin test with the dialysates of the Abderhalden reactions.

For the production of proteotoxin sterile sera were placed in sterile test tubes with sterile placental tissue (boiled) in the proportion of 1 gram of tissue to 2 c.c. of serum. These proportions were varied, however, in order to study quantitative factors upon proteotoxin production. Mixtures of serum and placenta were then incubated at 37° C. for eighteen to twenty hours when they were thoroughly centrifugalized to remove all particles of placenta and the serum carefully pipetted off. At the same time ninhydrin tests were made of the dialysates in the Abderhalden reactions. Cultures were made to check the technique, particularly since the sera were to be injected intracutaneously and intravenously.

Proteotoxin production was tested for by injecting intravenously varying amounts of serum into normal guinea-pigs of varying weights; also by the intracutaneous injection of serum into the skins of guinea-pigs and into ourselves, laboratory assistants and others who volunteered for the work.

The Abderhalden reactions were conducted after the dialysis method. All substrates were carefully prepared and only shells known by preliminary tests to be permeable to peptones and impermeable to whole protein were used. To 0.5 grams of substrate was added 1.5 c.c. serum and dialysis conducted in 20 c.c.

sterile distilled water. As usual serum and substrate controls were set up with each serum and in every test.

General Reactions. The results of the intravenous injection of sterile pregnancy sera incubated with sterile placental tissue for eighteen hours followed by thorough centrifugalization is shown in the following table:

TABLE 8.—Toxicity of Pregnancy Sera after Incubation with Placental Tissue.

Serum No.	Ninhydrin reaction.*	Test tube.		Weight of pig, gms.	Dose of serum, c.c.	Results.
		Placenta, gms.	Serum, c.c.			
1†	++++	3	6	630	4.0	Convulsions; died in two minutes.
2	++++	2	4	270	2.0	Very toxic; died in a few hours.
3	++++	4	12	350	3.5	Slightly toxic; recovered.
4	+++	4	6	470	1.0	No effect.
5	+++	3	7	210	2.4	No effect.
6	++++	2	4	300	2.5	Convulsions; died in two minutes.

* ++++ = strongly positive reaction (deep color).
+++ = moderately positive reaction.
++ = weakly positive reaction.
+ = weak or doubtfully positive reaction.
† Ninhydrin tests of dialysate of the serum controls were water-clear with all sera except Nos. 3 and 5 which showed a faint violet tinge due to dialyzable substances in the sera.

These experiments showed that the Abderhalden reaction is accompanied by the formation of toxic products capable of producing acute intoxication of normal guinea-pigs. Of those animals showing evidences of intoxication as hiccough, frequent passage of feces, prostration and minor convulsions, blood coagulation was delayed; two pigs succumbing almost immediately after injection showed the typical extreme emphysema of the lungs characteristic of anaphylactic death in this animal.

With many sera we were impressed with the fact that marked physical changes had occurred as shown by an opalescent or decided milky condition of the serum even after thorough and prolonged centrifugalization. As will be pointed out later these physical changes were less marked with other tissue substrates and indeed entirely lacking with sera treated with inorganic substances as kaolin and starch. Jobling, Eggstein and Petersen[30]

have reported, however, that the placental tissue is not digested but instead have found an actual increased resistance of the placental tissue to enzyme action.

Local Skin Reactions. The intracutaneous injection of these sera into guinea-pigs was found to produce local changes characterized by edema and superficial necrosis, erythema being less easily appreciated. A number of these were also injected into the skins of persons who volunteered for the tests and in these the erythema and infiltration were better marked.

All injections were made with the usual precautions to insure sterility and by means of a fine (No. 26) needle. In the guinea-pig skin these injections are made with some difficulty as it is necessary to inject into the layers of the skin rather than subcutaneously. The reactions were read at the end of twenty-four and forty-eight hours.

In practically all instances the degree of local toxicity of a serum was parallel with its general toxicity as shown in tables 8 and 9, and likewise followed the degree of digestion as evidenced by the amount of dialyzable substances detected with the ninhydrin reagent.

TABLE 9.—Local Skin Reactions, showing Toxicity of Pregnancy Sera after Incubation with Placental Tissue.

Serum No.	Ninhydrin reaction.	Test-tube.		Amount injected intracutaneously.	Result.
		Placenta, gms.	Serum, c.c.		
1	++++	3	6	0.05	Slight edema.
2	++++	2	4	0.1	Edema and superficial necrosis.
3	++++	4	12	0.1	Slight edema.
4	+++	4	6	0.1	Negative.
5	+++	3	7	0.2	Very slight edema.
6	++++	2	4	0.1	Well marked edema.
7	++	4	8	0.05	Volunteer; erythema 1.5 x 2.5 cm.; edema.
8	++++	3	7	0.05	Volunteer; faint erythema and slight edema.
9	+++	2	4	0.05	Volunteer; negative.
10	++++	1	3	0.05	Volunteer; erythema 1.5 x 1 cm.; slight edema.

Several of the guinea-pigs showing positive reactions were killed at forty-eight and seventy-two-hour intervals and at autopsy

the abdominal wall at the site of injection showed well-defined areas of gelatinous edema and acute congestion somewhat similar to the inflammatory edema produced by diphtheria toxin. One of our animals with a well-marked local reaction died in about seventy-two hours after injection.

These experiments having shown that human pregnancy serum develops marked toxicity when treated with human placenta, it was necessary to control the results with intravenous and intracutaneous injections of pregnancy serum alone.

To this end fresh human pregnancy serum was injected intravenously into several normal pigs within a few hours after bleeding and also after the sterile serum had been placed in an incubator for eighteen hours. In no instance were there any evidences of toxicity of sterile human pregnancy serum for the normal guinea-pig, either in a fresh active state or after incubation.

TABLE 10.—Sterile Pregnancy Serum is not Toxic.

Serum No.	Ninhydrin reaction.	Condition of serum.	Dose.	Local reaction.	Weight of pig, gms.	Dose of serum, c.c.	General reaction.
1	—	Incubated	0.1	Negative	210	2.8	Negative.
2	—	Fresh	0.05	Negative	300	2.5	Negative.
3	±	Incubated	0.2	Small nodule	250	3.0	Negative.
4	±	Incubated	0.1	Negative	450	3.8	Negative.
5	—	Fresh	0.2	Small nodule			
6	—	Incubated	0.05	Volunteer; faint erythema.			
7	±	Fresh	0.05	Volunteer; negative.			
8	—	Fresh	0.05	Volunteer; negative.			
9	—	Incubated	0.05	Volunteer; negative.			

Usually the intracutaneous injection of fresh pregnancy serum was without any effect whatsoever. If as much as 0.2 c.c. of fresh serum was injected strictly intracutaneously a small nodule with superficial necrosis of the epidermis not infrequently followed and this may be mistaken for an inflammatory reaction but with the injection of smaller amounts the chances of error were reduced to a minimum. A number of these injections are listed in Table 10. Four intracutaneous injections of sterile pregnancy serum in dose

of 0.05 c.c. both in fresh state and after incubation at 37° C. for eighteen hours into volunteers was followed by no disturbances in three persons and by a slight area of erythema with no appreciable edema in a fourth person. Regular Abderhalden reactions were conducted with these sera and the results with the serum controls shown in Table 10, three of the nine sera showing in the dialysates the presence of minute amounts of ninhydrin reacting substances.

The Toxicity of the Dialysate in the Abderhalden Reaction. The intravenous and intracutaneous injection of sera taken from the dialyzing shell at the completion of the Abderhalden reaction (20 hours at 37° C.) and thoroughly centrifuged showed that toxic substances were still present although usually diminished as compared with the same sera treated with placenta in test tubes in the same proportions.

For these experiments dialyzing shells were usually loaded with three to four times the usual amounts of placental tissue and serum and dialyzed against 20 to 30 c.c. of sterile distilled water. After twenty hours a ninhydrin test was conducted with 2 c.c. of the dialysate and the balance evaporated to one-third its original volume under sterile conditions.

The toxicity of these concentrated dialysates were then tested by a number of intravenous and intracutaneous injections in guinea-pigs. In most instances the results were negative. As shown in Table 11 two animals showed slight edema at the point of injection of 0.2 c.c. and one animal was rendered slightly toxic by the intravenous injection of 6 c.c.

TABLE 11.—The Local and General Effects of the Concentrated Dialysates of the Abderhalden Reaction.

No.	Ninhydrin reaction.	Dose intracutaneous.	Local reaction.	Weight of pig, gms.	Dose injected intravenously, c.c.	General reaction.
1	++++	0.05	Negative	300	6.0	Negative.
2	++++	0.2	Slight edema	450	7.0	Slightly toxic; recovered.
3	+++	0.1	Negative	400	5.0	Negative.
4	++++	0.3	Negative	370	3.5	Negative.

Intracutaneous injections of 0.05 to 0.1 c.c. of two of the concentrated dialysates into our own arms and those of six volunteers were followed by small areas of erythema in three instances.

These results would tend to show that the major portion of the toxic protein substances formed during the Abderhalden reaction do not dialyze through the shells ordinarily used in the usual interval of eighteen to twenty hours, although these dialyzable and ninhydrin reacting substances are somewhat toxic and probably constitute a portion of the proteotoxic substances produced. On the other hand they may represent cleavage products broken down beyond the stage at which they possess toxicity although still capable of giving the color reactions (ninhydrin and biuret).

Non-toxicity of Placental Peptone. As the dialyzable substances in the Abderhalden reaction are regarded largely as of the nature of peptones, amino-acids and other products of protein digestion, it is of interest to note that the intracutaneous injection of 0.1 c.c. of a 1 per cent. solution of placental peptone (Farbwerke-Hoechst Company) in normal salt solution and filtered through a sterile Berkefeld filter, was without any effect whatsoever, being non-irritant and if seized upon and digested in the skin left no evidences of this in the form of a local reaction.

These results in addition to those observed with concentrated dialysates tend to show that a portion at least of the toxic products of protein digestion are not dialyzable through tested shells in the usual period of the Abderhalden reaction.

Toxicity of the Serum in the Abderhalden Reaction is Increased with Reincubation. When pregnancy serum is removed from placenta after a period of eighteen hours in the incubator by thorough centrifugalization and is reincubated at 37° C. for for another period of twelve to eighteen hours toxicity is frequently appreciably increased as determined by intracutaneous and intravenous injections of the serum. As to the nature of the changes which may have taken place in the serum, our later experiments with inert substances as kaolin and starch show that the placental tissues probably deprives the serum of an antiferment and that

reincubation at 37° C. is followed by further autodigestion of the protein of the serum.

Among four controls consisting of sterile pregnancy sera alone incubated for thirty-six to forty-eight hours and injected intracutaneously and intravenously one developed an appreciable toxicity for the guinea-pig for the intravenous injection of 3.5 c.c. in a 280 gram animal was followed by prostration, lessened coagulation time of the blood and muscular twitchings with ultimate recovery.

II. Proteotoxin Production in Human Pregnancy Serum with Non-specific Tissue Absorbents

In order to test the specificity of the ferments in human pregnancy serum by the methods we were employing an extended series of experiments were conducted consisting in incubating sterile human pregnancy serum with various sterile substrates other than placental tissue as human kidney, sheep liver, dog liver and sheep muscle. These substrates were prepared in the same manner as placenta for the Abderhalden reaction and briefly boiled once more prior to the experiment in order to insure sterility.

Fresh sterile corpuscle free pregnancy serum was added to the various substrates in sterile test tubes in the same proportion as stated under previous experiments and incubated for eighteen hours. At this time the tubes were thoroughly centrifuged in order to remove all particles of tissue and a portion of serum used for intracutaneous and intravenous injection while a second portion was reincubated in sterile test tubes and tested sixteen hours later by the same methods.

At the same time regular Abderhalden reactions were set up with each serum and substrate and ninhydrin tests of the dialysates made eighteen hours later.

Except when a substrate of human kidney was used the degree of toxicity of the sera as shown by the intracutaneous and intravenous injection of the material was either less than that shown with placental tissue or entirely absent. Likewise while the

Abderhalden reactions showed some dialysable substances in the dialysates the amounts were less than occurred when placental tissue was used. In these tests however, human kidney frequently showed reactions of equal density and the sera of the other tests were found regularly toxic for animals. The results of a single set of these experiments are shown in Table 12.

TABLE 12.—Proteotoxin Production in Human Pregnancy Serum with Non-specific Tissue Substrates.

Serum No.	Substrate.	Ninhydrin reaction.	Local reactions.		Weight of pig, c.c.	General reactions.	
			Injected.	Result.		Amount injected.	Result.
16	Placenta	++++*	0.1	Positive	350	4.0 c.c.	Convulsions;died in two minutes.
16	Human kidney	+++	0.1	Positive	410	4.5 c.c.	Convulsions; died in a few minutes.
16	Dog kidney	+	0.1	Negative	380	4.0 c.c.	Negative.
16	Sheep liver	+ to ++	0.1	Negative	325	3.2 c.c.	Negative.
16	Dog liver	++	0.1	Negative	300	3.0 c.c.	Very slightly toxic;recovered
16	Sheep muscle	±	0.1	Negative	410	4.8 c.c.	Negative.
16	Human liver	+	0.1	Very slight edema	500	5.4 c.c.	Slightly toxic; recovered.

* Serum control of this particular serum showed a very faint violet color.

All of these substrates were used several times with several different pregnancy sera and while the results with all except human kidney were generally negative in several instances small amounts of toxic substances could be detected, especially after the period of reincubation and when the sera were injected in doses of 0.05 c.c. in the skin of our arms and those who volunteered for the tests. Intracutaneous injections into guinea-pigs did not appear to constitute as delicate a reaction and the intravenous injection of sera corresponding in amount to a cubic centimeter or more for each 100 grams of weight failed to indicate toxicity in sera showing slight local disturbances when injected into our own skins. In our experiments therefore toxic substances were regularly produced in mixtures of human pregnancy sera and placenta and human kidney and only occasionally with the other tissue substrates from the lower animals mentioned.

III. Proteotoxin Formation in Human Pregnancy Serum with Inorganic Substrates

We have treated human pregnancy serum with various inorganic substances including sterile kaolin, starch, agar and powdered quartz sand and tested the sera according to our methods after eighteen hours incubation and again after these sera had been freed of the absorbent by thorough and prolonged centrifugalization and reincubated for another period of sixteen to eighteen hours.

At the same time regular Abderhalden reactions were conducted with 1.5 c.c. of each serum and 0.2 gram of each of the absorbents. Particular care was exercised in having the serum and absorbent well mixed by means of gentle stirring with a sterile rod.

In the test tube the proportions of serum and absorbent were 0.1 to 0.2 gram absorbent to each cubic centimeter of serum.

The results of two sets of these experiments with two different sera are shown in Table 13. The injections were of sera removed from the absorbents after eighteen hours incubation at 37° C.

Table 13.—Proteotoxin Formation in Human Pregnancy Serum with Inorganic Absorbents.

Serum No.	Absorbent.	Ninhydrin test.	Local reactions.		Weight of pig, c.c.	General reactions.	
			Dose.	Result.		Dose, c.c.	Result.
18	Kaolin	—	0.05	Negative	400	4.2	Negative.
18	Starch	±	0.05	Negative	510	5.0	Negative.
18	Agar	+	0.05	Faint erythema	385	4.0	Slightly toxic; recovered.
18	Quartz	±	0.05	Negative	0	0	0
19	Kaolin	±	0.05	Faint erythema	280	2.8	Toxic; died during night.
19	Starch	++	0.05	Erythema 1.5 x 1 cm.	300	1.8	Slightly toxic; recovered.
19	Agar	++	0.05	Negative	0	0	0
19	Quartz	±	0.05	Negative	0	0	0

Ninhydrin test of serum control dialysate of serum No. 18 was water-clear, of serum No. 19 a faint violet color.

The local reactions listed are those observed twenty-four hours after the intracutaneous injection of 0.05 c.c. of the sera into the arms of volunteers and ourselves. A number of injections of 0.1 c.c. into the abdominal skin of guinea-pigs yielded negative or at most inconclusive results.

After reincubation of the sera alone for a second period of sixteen hours an increase in toxicity was apparent in several instances but in the majority the results of injection were purely traumatic or clearly negative. In one instance where marked intracutaneous and general reactions were observed in guinea-pigs the serum was found contaminated with bacteria and special precautions against contamination were necessary.

We must also record the observation that these sera were usually quite clear or at most but slightly opalescent after separation from the absorbents, an appearance quite in contrast to the opacity and milkiness of sera digested with placental or human kidney tissue.

The results of these experiments showed that when inert substances as kaolin, starch and powdered quartz are added to human pregnancy serum and the mixtures are incubated for sixteen to eighteen hours toxic substances are produced but that these are either much less in amount than that formed in the presence of placental tissue or else they are not toxic for the human skin or guinea-pig. In view of the results of our experiments previously given the latter assumption has no weight. We believe that thorough centrifugalization of the sera removed all particles of the absorbents used; the starch mixtures however, were somewhat more troublesome in this respect.

Of these absorbents agar rendered more toxic sera yielding positive cutaneous reactions than kaolin or quartz and starch came second in the number of sera rendered toxic; in the former protein substances in the agar may have aided in the processes of proteotoxin production and in the latter minute particles of starch in a colloidal state of division may have aided in producing local reactions in a traumatic manner.

IV. Proteotoxin Formation in Human Male Serum with Placental Tissue

As controls in the work and for the purpose of studying the specificity of ferments in pregnancy serum, a similar series of experiments were conducted with fresh male serum using placental tissue as well as other tissue substrates and the inorganic substances as kaolin, quartz, etc.

These experiments were conducted in exactly the same manner as those already described. Usually in every experiment with pregnancy serum a male serum was used at the same time, with the same substrates or absorbents and tested for toxicity by intracutaneous and intravenous injection in the same manner. Abderhalden reactions were set up at the same time and the dialysates tested with ninhydrin. In this manner we were able to compare the toxicity of the sera by intracutaneous and intravenous injection with the occurrence and degree of protein digestion as shown in the ninhydrin reactions.

Sera were usually obtained by securing blood from the veins of healthy male assistants in the laboratory and from our own arms, all bleedings being conducted in such a manner as to insure sterile products. As with the pregnancy sera these were used within three hours after collection and their toxicity tested after eighteen hours incubation with the substrates or absorbents and again after reincubation for sixteen hours following removal of the absorbent by prolonged centrifugalization.

The results of some of these experiments are shown in Table 14 where the results of the Abderhalden reactions and the local and general reactions of sera after primary and secondary incubation are shown in parallel columns.

All intracutaneous injections with dosage of 0.05 c.c. were into the arms of volunteers and ourselves; all others into the abdominal skins of guinea-pigs.

Briefly the results were somewhat similar to those observed with the pregnancy sera. Of the tissue absorbents or substrates toxicity formation was most apparent with kidney and placenta

TABLE No. 14.—Proteotoxin Production in Male Serum with Various Organic and Inorganic Substrates or Absorbents

Serum No.	Absorbent.	Ninhydrin reaction.	Local reactions.			General reaction.					Result.
						After 18 hours incubation.			After reincubation.		
			Dose.	After 18 hours.	After reincubation. 16 hours.	Wt. pig, Gms.	Dose.	Result.	Wt. pig.	Dose.	
1	Placenta	+	0.2	Slightly positive	Positive	530	4	Died over night	460	4	Died over night.
2	Human kidney	+	0.2	Marked positive	Positive	410	4	Toxic, recovered	400	4	Convulsions, recovered.
2	Placenta	+	0.2	Negative	Slightly positive	430	4	Negative	400	4	Very slightly toxic.
2	Human kidney	+	0.2	Negative	Marked edema	430	4	Convulsions, recovered	380	4	Died in 2 minutes.
3	Placenta	±	0.1	Negative	Slight edema	400	2	Negative	0	0	0
4	Placenta	—	0.2	Negative	Negative	0	0	0	500	4	Convulsions, recovered.
4	Human kidney	+	0.2	Negative	Very slight edema	0	0	0	480	4	Convulsions, died in 36 hours.
5	Placenta	±	0.05	Negative	Positive	560	0.8	Negative	400	2	Negative.
6	Placenta	+	0.05	Negative	Negative						
6	Human kidney	+	0.05	Erythema 1.5 x 2 cm.	Same						
6	Dog liver	+	0.05	Negative	Negative						
6	Sheep liver	+	0.05	Negative	Negative						
7	Placenta	+	0.05	Erythema 2.0 x 2.5 cm.	Same						
7	Placenta	+	0.2	Slight edema	0						
7	Human kidney	+	0.2	Edema	0						
7	Kaolin	—	0.05	Negative	Negative						
7	Starch	—	0.05	Negative	Negative						
7	Agar	+	0.05	Slight erythema	Erythema						
8	Kaolin	±	0.05	Faint erythema	Same						
8	Starch	±	0.05	Negative	Negative						
8	Agar	+	0.05	Faint erythema	Erythema						

Ninhydrin tests with dialysates of sera 1, 2, 3, and 8 were water-clear; with sera 4, 5, 6, 7 a faint violet.

All intracutaneous injections with dosage of 0.05 c.c. were into the arms of volunteers and ourselves; all others into the abdominal skins of guinea-pigs.

whereas with other tissues as dog liver and sheep liver toxicity was not apparent or present in but slight degree.

The sera of healthy males however contain ferments which when released bring about protein digestion and the formation of proteotoxins and while this phenomenon was most marked with tissue substrates it also occurred occasionally and to a slight degree with kaolin and agar.

Practically all of those sera were tested for toxicity for the guinea-pig without the addition of any absorbent. Fresh male serum is not toxic for this animal either by intracutaneous or intravenous injection although of six sterile sera incubated at 37° C. for thirty-six hours, one produced edema upon intracutaneous injection and 2.5 c.c. injected intravenously into a 380 gram pig was followed by convulsion and death a few hours later.

V. The Relation of Complement to Proteotoxin Production in Vitro

The relation of complement to the mechanism of the Abderhalden reaction has attracted considerable attention mainly in attempts to establish the identity of the "protective ferments" with the cytolytic amboceptors of Ehrlich. Williams and Pearce[31] found that inactivation of a pregnancy serum impaired but did not entirely remove its digestive capacity and Lange[32] and others have recorded similar observations. The experiments of Stephan,[33] Hauptmann,[34] Bettencourt and Menezer[35] and Steising,[36] however, seem to show a relationship of complement to the Abderhalden reaction in as much as the addition of the serum complements of the guinea-pig, rabbit or human male seem to reactivate a serum inactivated by heating at 56 C. for half an hour. Jobling, Eggstein and Petersen[37] have shown that serum complement and normal proteolytic ferments are not identical and that while the former may be inactivated by heating at 56 C. for half an hour the latter are more resistant, the results observed following the addition of serum complement to inactivated pregnancy

serum being ascribed to the amounts of non-specific protease thereby added.

Abderhalden has found that the addition of a serum complement appears to play a part in the mechanism of the reaction but hopes to find an explanation that would remove the relation from the realm of the side chain theory of Ehrlich. The explanation offered by Jobling and his colleagues would appear to be satisfactory and is based upon experimental evidence.

In a series of experiments we have digested pregnancy and male sera with human placenta, human kidney, sheep liver and kaolin both with fresh active sera and with the same sera heated at 56° C. for one-half hour. While the ninhydrin reactions with the dialysates of the Abderhalden reactions with the inactivated sera and substrates were usually weaker than when fresh active sera were used, still heating under these conditions did not entirely prevent the formation of dialysable substances in a mixture of pregnancy serum and placental tissue. The results of the intracutaneous and intravenous injections of these heated and fresh sera after digestion with various substrates into guinea-pigs and into our own arms showed even less difference especially after a second period of incubation following the removal of the substrate by centrifugalization.

We have also added fresh guinea-pig serum complement to inactivated pregnancy serum in the proportion of 0.5 c.c. complement to 1.5 c.c. pregnancy serum and allowed digestion to occur in the incubator for eighteen hours in the presence of various organic and inorganic substrates and absorbents. The intracutaneous and intravenous injection of these sera showed in a few instances a slightly higher degree of toxicity but in the majority of cases resembled in this respect the same sera to which guinea-pig serum had not been added. The Abderhalden reaction, however, showed more marked difference in so far that the ninhydrin reactions were usually stronger in the former.

From these experiments we conclude that while fresh sera are more active than heated sera this increased activity is not due to the presence of complement in the sense of our conception of its

role in the side chain theory of antibodies, but rather that the results of the addition of serum complement are due to the normal proteolytic ferments thereby added.

SUMMARY OF PART II

1. Proteotoxins are produced during the Abderhalden pregnancy reaction, which, when injected intracutaneously and intravenously into normal animals produces local and general changes analogous to anaphylactic reactions.

2. Proteotoxins produced in a mixture of human pregnancy serum and human placenta are toxic for normal guinea-pigs.

3. The ninhydrin test with dialysates and intracutaneous and intravenous injections of the sera in the Abderhalden reactions yielded fairly parallel indices of the degree of protein digestion and proteotoxin production.

4. The addition of various tissue substrates other than placenta to human pregnancy serum was followed occasionally by proteotoxin production as shown by intracutaneous and intravenous tests with the serum but except when a substrate of human kidney was used the amount of proteotoxin produced was usually much less than that produced in mixtures of pregnancy serum and human placenta. Similar results were observed with inorganic absorbents as kaolin, starch, quartz, etc.

5. The proteolytic ferments in healthy normal serum may produce small amounts of proteotoxins when tissue substrates are added and occasionally and to less degree with inorganic absborbents as kaolin and starch.

6. Complement in itself has no direct relation to the ferments in pregnancy serum. Inactivation of serum probably reduces its digestive power through destruction of a normal proteolytic ferments and reactivation of a serum by means of the addition of serum complement increases its digestive power to a slight degree probably by reason of the addition of these normal ferments.

7. In pregnancy serum there are two sets of proteolytic ferments normal and non-specific and specific ferments. The former may

be released through absorption of the antiferment by means of various nonspecific organic and inorganic substances whereas the latter are released through the absorption of the antiferments by means of the specific protein antigen alone.

8. Our experiments also suggest that the protein matrix in the Abderhalden reaction is not only the protein of the serum but also to some extent as that of the tissue substratum itself.

GENERAL DISCUSSION

While we have naturally hesitated to report upon these local skin reactions in pregnant and puerperal women until a relatively large number were studied in view of the contradictory results obtained by others, we feel justified in concluding that the reactions were anaphylactic in nature and due to an anaphylatoxin produced by the action of general ferments upon a protein substrate.

We have not been primarily interested in the question of the practical diagnostic value of a skin test for pregnancy and have merely recorded the results as observed. We do not believe at present that this reaction possesses a practical value in diagnosis, certainly not among women who have borne children.

According to the experiments described in part two, pregnancy serum contains proteolytic ferments which when rendered active *in vitro* produced toxic substances capable of inducing local and general reactions analogous to those observed by Vaughan, Friedberger and others and regarded as anaphylactic in nature. These observations support the views expressed in part one of this paper, concerning the probably anaphylactic nature of the reactions following the intracutaneous injections of *placentins* and *nephrins* although these occurred to some extent in non-pregnant women and men and in this manner lacked absolute specificity. It is highly probable that the process of proteotoxin formation in the skin (*in vivo*) is identical with that occurring in the test-tube (*in vitro*).

Our experiments also suggest that in pregnancy serum there are two sets of proteolytic ferments, one composed of normal

non-specific ferments and the second of more or less specific ferment. While the latter may not be specific in the sense of absolute digestive power for placental protein alone yet it appears to be rendered active in the presence of placental tissue, to a much lesser extent or not at all by other human tissues and those of lower animals and practically not at all by inorganic substances.

Our experiments are, however, in accord with those of Jobling and Petersen, Plaut, Peifer, Bronfenbrenner and others to the extent that inorganic substances as kaolin are capable of releasing the normal tryptic activity of a serum probably through the absorption of antiferment followed by the digestion of serum protein. Our work indicates that this action is non-specific and the result of the release of normal proteolytic ferments whereas the activity of the specific ferments in pregnancy serum are best in evidence in the presence of placental tissue. These results are in accord with those of Bronfenbrenner[38], who found that the Abderhalden test is more or less specific as based upon the theory that removal of the antiferments depends upon a change of the colloidal conditions of the serum resulting from the specific combination of the antigen of the substratum with an antibody of the patient's serum, the serum derived of the antiferment in this manner undergoing a process of autodigestion.

It is probable, therefore, that the Abderhalden reaction is an anaphylactic reaction *in vitro,* insofar as its mechanism is concerned. For the reason that normal human sera contain variable amounts of proteolytic ferments it is reasonable to expect that the intracutaneous injection of protein material into the skin may in a small percentage of persons be followed by a local reaction due to non-specific proteotoxin production. In view, however, of the high specificity of anaphylactic reactions one cannot explain the mechanism of anaphylaxis and production of anaphylatoxins upon simple absorption of antiferments alone without the assumption at least that specific antibodies or ferments are produced after the parenteral introduction of proteins and that these are released through absorption of the antiferments by means of the specific protein antigen alone.

With the Abderhalden reaction as now conducted it seems impossible to avoid a certain percentage of non-specific reactions due to the presence of non-specific proteolytic ferments. A means of removing these preliminary to the main test for specific ferments will probably render the reaction more specific within wider quantitative limits.

While numerous investigations indicate that the protein matrix is the serum protein itself we cannot at present subscribe to this view and exclude the tissue substrate entirely as a second matrix; rather we are still inclined to believe that in addition to digestion of serum protein the tissue substratum is likewise attacked and adds to the production of proteotoxic substances.

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THE VALUE OF SCIENTIFIC DOUBT IN SURGICAL DIAGNOSIS[1]

By JOHN B. ROBERTS, M.D.

Massive Intrahepatic Hematoma from Rupture of Hepatic Vein

I operated last winter upon a colored man, aged fifty-one years, who had fallen and struck the epigastric region against a step. When seen by me a few hours after the accident he was suffering intense pain in the upper abdomen, and the muscles of the anterior abdominal wall were rigidly contracted. There was only a slightly increased pulse rate, with normal respirations. The temperature was somewhat subnormal. He had, however, the peculiar ashy hue of pain and shock, recognizable even in the negro countenance.

My diagnosis was rupture of stomach or intestine, and I advised immediate operation because his evident suffering, although morphin and atropin had been given hypodermically, proved the existence of a serious lesion.

On opening the abdomen I found a little free blood in the peritoneal cavity, extravasated blood within the gastrohepatic omentum and the transverse mesocolon, and also under the peritoneum covering the attached side of the colon. No rupture of stomach or bowel was discovered. Liver, spleen, intestines, gall-bladder and urinary bladder seemed free from injury. Some blood was discovered behind the peritoneum near the pancreas but this and the other extravasations were not accomplished by evidence of free bleeding anywhere.

[1] Read June 2, 1915.

The abdominal wound was therefore closed and my diagnosis of ruptured hollow viscus remained unconfirmed. The man died as the operation was finished either from shock or from ether poisoning due to careless administration.

Autopsy at first showed nothing definite, except the findings seen at the operation, although the abdominal and the thoracic contents were removed. There were small subpleural extravasations and extravasations under kidney capsule.

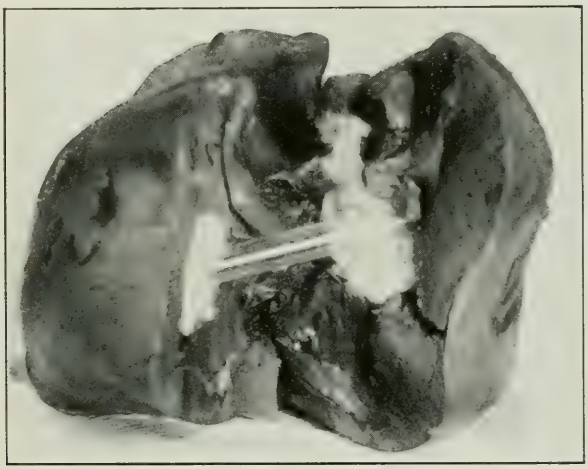

Fig. 1.—Traumatic rupture of fatty and somewhat cirrhotic liver, upper surface. Cavity, which was occupied by a massive intrahepatic hematoma, is filled with cotton, incised right lobe held apart by a glass tube.

After further search for the source of the hemorrhage had been considered almost unnecessary, I split open the removed liver and found a blood-clot, of about six fluidounces, lying in a cavity within the right lobe of the liver at its posterior part, close to the entrance of the hepatic veins into the cava. The largest of the three veins was torn about an inch from cava by an opening about a sixteenth of an inch long.

Dr. John A. Kolmer found the liver to be markedly fatty with slight perilobular fibrosis, and no evidence of trepanoma pal-

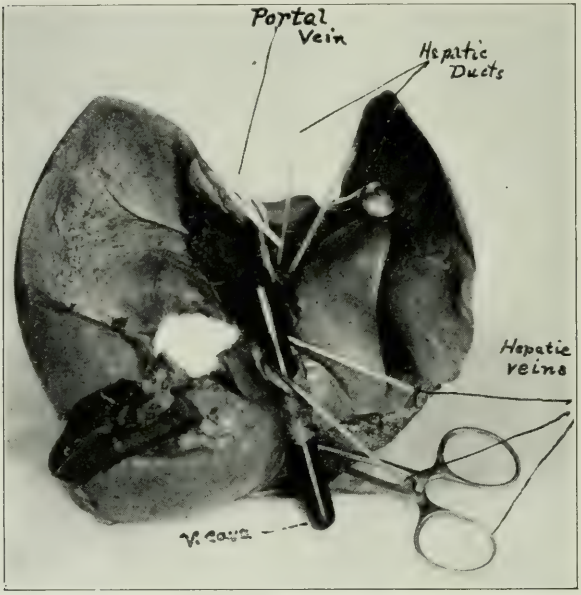

FIG. 2.—Lower surface of same liver in which a massive traumatic intrahepatic hematoma was found at the back of the right lobe; it was from rupture of the largest hepatic vein about an inch from its opening into the vena cava. Black rubber tube in vena cava; hemostatic forceps in injured hepatic vein; twisted wire in portal vein; match sticks in hepatic ducts and the two uninjured hepatic veins.

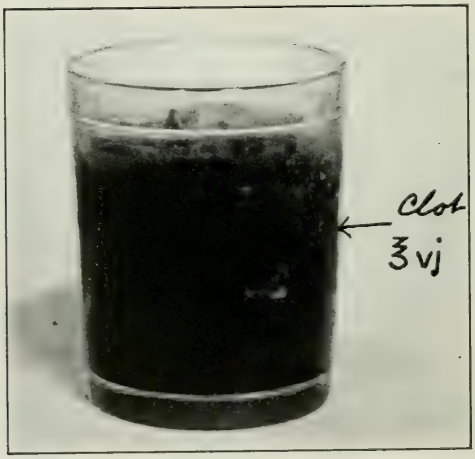

FIG. 3.—An ordinary glass tumbler containing clot, removed from the interior of the liver, due to traumatic rupture of the most posterior hepatic vein. The clot measured about 6 fluidounces.

lidum. The cavity containing the soft dark clot was irregularly lobulated at the widest part about 3 inches in diameter.

This intrahepatic rupture with hematoma, a rare lesion, was an unthought-of injury. Its preoperative diagnosis was impossible, but its possibility should have been suspected when I saw, before death, bloody infiltration in the gastrohepatic omentum.

Horseshoe Kidney Simulating Perforating Appendicitis

In the same month I was asked to see a boy, aged sixteen years, with appendicitis. He had been seized with severe abdominal pain in the morning with vomiting. He had very little if

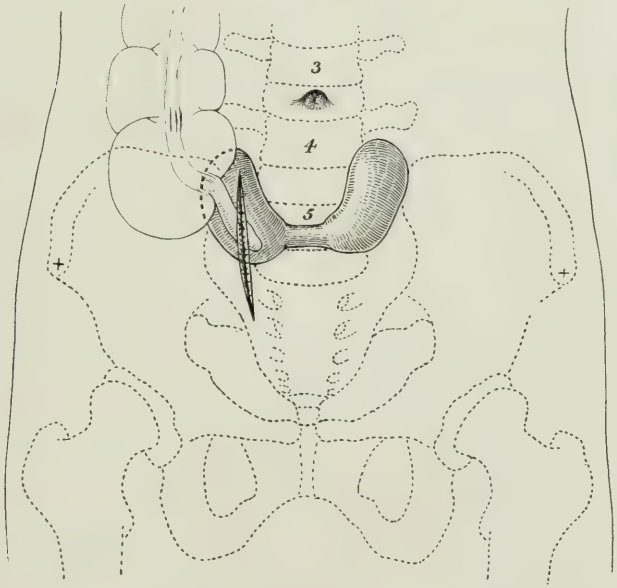

Fig. 4.—Congenital horseshoe sacral kidney simulating appendicitis.

any abdominal rigidity, but there was a very palpable mass in the right inguinal region a little lower than McBurney's point and some increase in leukocyte count. Temperature and pulse were not far from normal.

I would have delayed operation for further observation of the patient had not the superficial and readily palpable mass convinced me that perforation of an inflamed appendix had occurred, and that the suppurating organ was plastered by adhesive lymph against the internal surface of the belly wall and that it was probably surrounded by an abscess.

After hasty sterilization of the skin the abdomen was opened, and an unadherent normal-looking appendix removed. It was lying immediately over the right lower pole of a horseshoe kidney. The left segment of the double kidney was felt with my fingers in the abdomen. It was attached to the kidney visible under the appendix by a flat, fibrous band about an inch in width. This connecting bridge lay across the spinal column at about the level of the lumbosacral intervertebral cartilage and joined the two renal organs at their lower ends.

The four-inch vertical wound in the rectus was closed, and no trouble ensued, except delay in union by reason of superficial suppuration. Microscopic examination showed, according to Dr. Kolmer's report, evidence of chronic interstitial appendicitis.

To find a horseshoe kidney so low in the abdominopelvic cavity is rather rare. For it to simulate an appendicular abscess is a combination of symptoms of exceptional occurrence.[1] The history of this patient proves that hasty diagnoses are not always reliable.

Other Operative Errors

Reflection upon the unusual cause of diagnostic error in these two cases has induced me to make some statements on the value of a doubting mind in surgical practice and to confess the unreliability of my snap diagnoses.

A certain surgical author has recently said, "diagnosis by intuition is a rapid method of reaching a wrong conclusion." Some experiences within the last few months have convinced me

[1] Dr. M. S. Kakels has reported an instance of "Sacral Kidney," simulating acute appendicitis, in Medical Record, December 21, 1912.

that this statement and that of another master, who said, "none of us is infallible, not even the youngest," deserve to claim our respectful consideration.

Doubt may be present in a surgeon's mind because of a limitation of personal knowledge, a careless application of the knowledge he possesses, a limitation of time, due to the urgency of symptoms, or an absence of general professional knowledge of the physiology and anatomy of the human organism. I have on various occasions hesitated to operate from all of these causes, but am hoping that the second mentioned, carelessness, has been an infrequent influence.

The tendency nowadays seems to be to operate when in doubt without devoting much time to exercising one's faculties in diagnostic queries. A usual gynecological notice on bulletin boards seems to scoffers to be "abdominal section," often abbreviated to "section." In former days "section" meant, I believe, "an autopsy." Now it is used, I suspect, to cover "reserved diagnosis," and not a multitude of "sins of omission" in clinical examination.

A medical visitor from Europe, a few years ago, wrote that in America patients were always in such a hurry that they were unwilling to accept medical treatment for their ailments but insisted on being subjected to surgical operations. All thoughtful lovers of the science of surgery must recognize this attitude of mind in many of their patients. It is a reflection of the imaginary safety of aseptic technic, under all circumstances in all conditions of men. In my earlier surgical life I have smelled the odor of rotting pus every morning as soon as the door of the surgical ward was opened for my admission. Many ounces of pus have I, day after day, pressed out of cavities in infected tissues surrounding the necrotic bones of open fractures; while the injured sufferers gradually faded until amputation opened the way to slow months of convalescence or quickly dropped into the grave from septic infarctions or repeated secondary hemorrhages.

No one, therefore, more than I realizes the ineffaceable debt owed to Lister; but that debt does not close my mind to the

needless mutilations and unnecessary deaths due to the insane rush to operative therapeusis by the ignorant public, induced, thereto, because the saving grace of doubt seldom enters into the mind of some dogmatists of surgical art.

John Hunter's definition of surgery was that it consisted in curing a disease rather than in the removal of it by mechanical means. An earlier writer put the same thought in Sanscrit thus (*Art of Life*): "Only the association of medicine with surgery forms the perfect physician. The physician who is deficient in the knowledge of one of these branches resembles a bird with but one wing."

Thomas Vicary, "sergeant chyrurgion" to Henry VIII, explains in the *Profitable Treatise of Anatomy*, of 1548, "what properties and conditions a man must have before he be a perfect chirurgion." "The first (I sayde) he ought to be learned and that he knowe his principles, not onely in Chirurgerie but also in Phisicke, that he may the better defende his Surgery; Also he ought to be seene in natural Philosophie, and in Grammer, that he speak congruitie in Logike, that teacheth him to prove his proportions with good reason. In Rethorike, that teacheth him to speak seemely and eloquently; also in Theorike, that teacheth him to know thinges naturall, and not naturall, and thinges agaynst Nature. Also he must know the Anatomie, for al Authors write against those Surgions that worke in mans body not knowing the Anatomie, for they be likened to a blind man that cutteth in a vine tree, for he taketh more or lesse than he ought to doo."

Many present-day operators would find it difficult to defende their Chirurgerie upon the principles of "phisicke" and of "chirurgerie" by speaking in "logike, that teacheth them to proue their proportions with good reason." Some indeed, in my opinion, when cutting patients, do take away more than they "ought to doo."

The mind that admits no doubt is a closed door; useful in emergency at times, I admit, but dangerous to the public. Its dogmatism often quickly brings the wavering patient under its sway and may thus occasionally save a man from the risks of delay

borne of timidity. Who, however, can number the fatalities due to hasty diagnoses upon which unnecessary operations have been undertaken?

The relative safety of aseptic wounds has led to a wide distribution of operative surgery, but has taken a great toll in deaths by its encouragement of hasty diagnoses and an unhesitating resort to mutilating therapeusis.

I once heard an enthusiastic surgeon when asked how much liquid paraffin he gave to test the presence of obstinate intestinal stasis, reply, "As much as she will take." The indefiniteness of the response was equal to the illogical determination that removal of the entire colon was the only cure. The effect of a dose based on the patient's willingness to swallow was apparently the only proof of the medical incurability of her probable static constipation. One might as well practise surgery on the theory that a pain in the abdomen requires ablation of the appendix, whenever the patient will permit an incision to be made in his abdominal wall.

Too much trepidation in the surgeon's mental equipment is not what I suggest but a care-taking investigation before the diagnosis is announced, based on a doubting, thoughtful review of personal and family history and of physical and psychic symptoms. Then a balancing of the operative risks with the dangers of a reasonable delay should influence the surgeon's resort to immediate operation.

Fractures

The present-day addiction to operative treatment of fractures is a case in point. A brilliant young surgeon, for instance, recently informed me of his position on this question in these words: "I operate on every case of fracture of the femur, most cases of fracture of the tibia," etc. There is no suggestion of possible doubt in that statement. Hence, I dislike it. It is not scientific; it is simply dogmatic. The subcutaneous fractures, which require blood-shedding treatment, are those which cannot be reduced properly otherwise, and those in which the reduction cannot be maintained except by direct fixation.

The wisdom of doubt about such general resort to operative intervention in fractures has been impressed upon me by experiences like the following: A boy, aged twelve years, fell on shipboard and sustained an oblique fracture of the left femoral shaft

FIG. 5.—Spiral fracture of right femur occurring on shipboard. M. D., boy of twelve years. Treated by Buck's traction method; *x*-ray taken soon after injury.

in its lower half. For a week he was treated in the ship at sea, on a sofa berth, by traction, then encased from umbilicus to ankle in plaster of Paris and transported over a hundred miles by train to a hospital. There he was treated by Dr. John H. Gibbon by

Buck's extension method. A few days ago, about twenty months after the accident, he was examined by me, and it was difficult to tell which leg had been injured. He had perfect function and so little shortening that it was difficult to determine whether it

FIG. 6.—Spiral fracture of right femur, boy M. D., twelve years old, treated by Buck's traction method. There is scarcely any shortening, but perhaps a little outward bending. Photograph taken about twenty months after the injury.

exceeded a quarter-inch. The boy was active, straight in spine, and was the captain of the junior tennis team at school.

About eighteen months ago a tall young man, aged sixteen years, standing on a coasting sled, was obliged to jump off. He received a spiral fracture of the shaft of the femur, with the separation of a triangular piece of bone in addition to the chief

line of fracture. He was treated with Buck's traction by Dr. T. F. Branson and Dr. E. B. Hodge. The fracture was so long that the callus made his thigh bone feel like a massive column within the integument of his thigh. I examined him carefully recently, finding about a half-inch shortening, a slight lateral deviation

FIG. 7.—Spiral fracture of the shaft of the left femur, with a large triangular fragment detached. A. D., sixteen years.

of the spine, easily corrected by elevation of heel within the shoe, and perfect function.

Both of these patients, in my opinion, have been treated more scientifically and more reasonably than if their parents had been induced by an operative "addict" to permit fixation with metal

plates. The type of fracture in both instances was that which is claimed to often need direct fixation to get good results. The anxiety, anesthesia risk, and other unnecessary possibilities of harm appertaining to open blood-letting treatment was not justified in either of these cases. They are mentioned here because I had opportunity of seeing the cases during and after treatment, and, in fact, had some part in the management of them.

FIG. 8.—A. D., sixteen years, after treatment by Buck's traction method. There is slight shortening of the left lower extremity, easily corrected by a pad under the heel inside the shoe. Photograph taken about eighteen months after the injury.

Advocates of the open treatment of fractures, as superior to the non-operative routine, base much of their argument on the reliability of radiography as indicative of offending displacement. Radiograms are of exceeding value in confirming the existence of fracture in doubtful injuries, but the degree of displacement may be in some degree factitious both affirmatively and negatively.

The position of the tube, its distance from the limb, and the distance of the examined bone from the photographic plate vary the shadow picture greatly.

FIG. 9.—Inversion fracture of tibia and fibula at the ankle in a man, showing little deformity in the *x*-ray plate. Anterior view, The deformity was marked and overcome only with difficulty under ether.

The radiologist as well as the surgeon must be ever on his guard to avoid errors from false readings of the shadow values. Recently I have treated several fractures, the radiograms of which were reported to show good position, when clinical inspec-

tion showed to anatomical eyes that there was marked displacement. This was so notwithstanding that the *x*-ray plates were taken in two planes and read by an expert in skiagraphy. One case

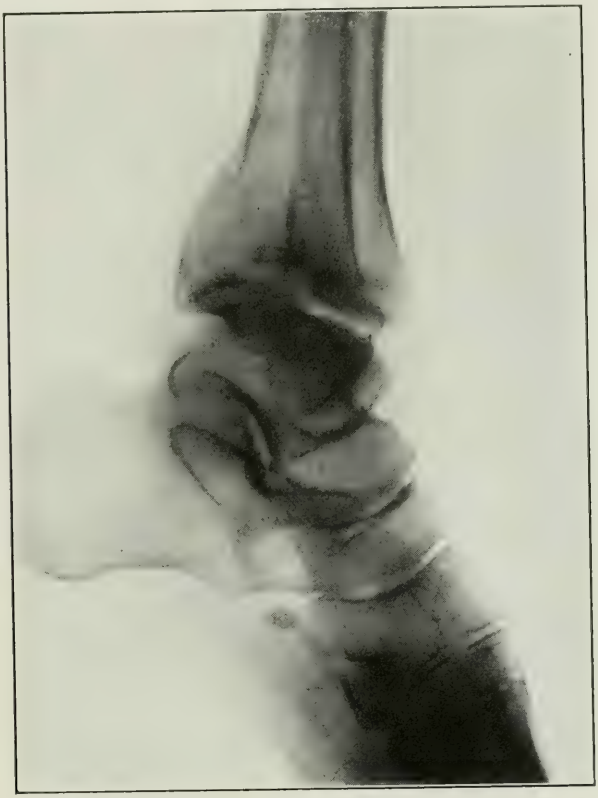

Fig. 10.—Inversion fracture of tibia and fibula at the ankle in a man, showing little deformity in the *x*-ray plate. Lateral view. The clinical deformity, inversion and retraction of foot with impaction, was marked and was overcome with some difficulty under ether.

was a man with inversion fracture of the tibial and fibular malleoli with backward and inward displacement of the foot, requiring great force under ether to break up displacement and obtain reconstruction. The other was a green-stick fracture of radial and

ulnar shafts that required complete fracture of both infractions to restore the gross contour of the forearm.

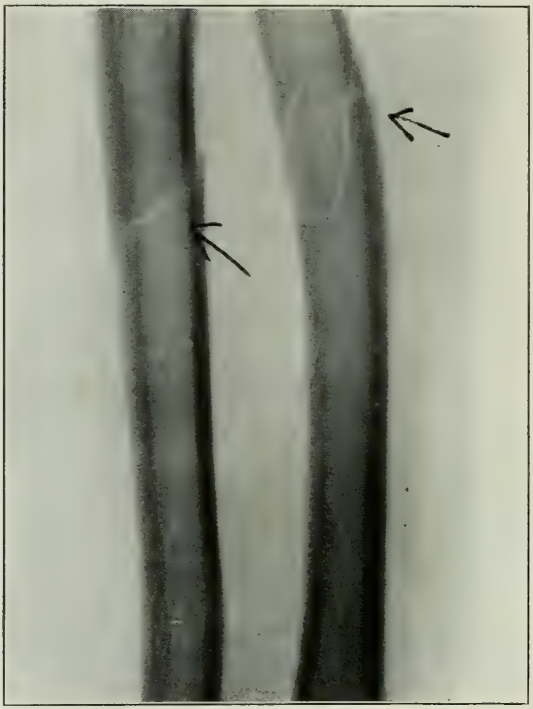

FIG. 11.—Fracture of both bones of the forearm (green-stick) in a boy, showing little deformity; though marked clinical deformity requiring refracture under ether was present.

OPERATIVE RISKS IN ABDOMINAL SURGERY

Some years ago I was consulted by a woman, about twenty years old, who said that she had been informed that she had had appendicitis, and that now was the time for an interval removal of the offending organ. She wanted my opinion before submitting. After careful investigation I replied that an interval operation was justifiable if a competent surgeon was employed. I heard no more of the patient until some months later, when I learned that she

had died apparently of hemorrhage a few hours after operation done in a hospital.

A few weeks ago I operated on a young man in desperate condition from tight intestinal constriction, secondary to an appendicitis operation with removal of the organ performed a half-year previously. He fortunately recovered, though there was opaque serum in the peritoneal cavity and much congestion of the strangulated ileum.

I recently saw a man with bronchopneumonia which developed after an exploration of the abdominal cavity for possible intestinal wounds following a knife thrust into the belly wall. No visceral injury was found. Many sequels of abdominal operation such as hemorrhage, intestinal obstruction, and ether poisoning, will probably be remembered by this audience.

I met some years ago in an elevator a vigorous-looking man who called me by name and proved he was a man who would have had a leg amputated a couple of years before had I not urged his surgeon to keep applying more skin grafts. The oldest patient I ever had with appendicitis died at 85 years from pneumonia. I had attended him about six years before with a well-marked appendicitis and advised non-operative treatment. The decision was evidently judicious.

Unnecessary Mutilation of Women

A few weeks ago a woman with a small almond-size growth in one breast came to me in great trepidation because after a bruise she had discovered the little nodule. She was about thirty-eight years old, and had consulted a surgeon who insisted that she must lose the entire breast by amputation. My opinion was given that the nodule should be removed by operation and subjected to microscopic study before such a disaster came upon her. I excised with a few sweeps of the knife the growth and a considerable block of surrounding gland tissue. Dr. John A. Kolmer reported that the growth was a fibrocyst adenoma, with no evidences of malignancy. I append his report in full:

"I beg to report that sections of the tumor of the mammary gland which you recently submitted for examination show the histological structure of a fibrocyst adenoma, with no evidences of malignancy. The fibroma predominates and is of a hard variety. I suspected chronic cystic mastitis, but there is not sufficient evidence of the chronic inflammation. There is, in my opinion, a numerical increase in the glands, and many are cystic, due, I believe, to a constriction of their ducts by the increased amount of fibrous tissue. As already stated, careful examination of these glands and ducts does not disclose any evidence of malignancy."

About two and a half years ago a school-girl, aged seventeen years, found a small nodule in her breast. I acted in a similar manner. In this case the opinion of a skilled microscopist was that there was some evidence of potential malignancy in the histological structure of the sections made. His opinion was supported by two other microscopists. A third to whom I submitted the sections believed that the growth was one of those improperly considered malignant. After much thought I concluded to excise the scar of the little incision and remove a good-sized wedge of the breast. The patient has been seen since at intervals without any evidence of return, and reported to me orally a few days ago that nothing had appeared to suggest trouble.

Surely in both these cases the results have shown that a doubting mind and a willingness to use pathology and clinical experience as coördinate assistants are better attributes of a surgeon than an operative dictum that potential trouble shall lead to immediate sacrifice of organs despite the risks physical and the agonies psychic of patient and family.

Enucleation of Healthy Tonsils a Wrong

The bloody sacrifice of entire tonsils which has recently been offered to the écraseur, tonsil punch, and other pharyngeal instruments seems to me unworthy of scientific medicine. Who knows for certain the value or the worthlessness of these lymphoid

organs in the little child's throat. I see frequently a healthy, fine-looking mother of several children, who in early life was my patient with middle-ear inflammation and enlarged tonsils. I advised shaving off the redundant tonsillar tissue with a tonsillotome, as was the custom of the time. The parents never consented, and therefore no operation was done. The child grew to womanhood and married. She has had no trouble with ears or throat, but is unusually healthy in every way.

A few years ago one of her children died in five days with a violent infection, shown at autopsy in brain and spinal cord, only a few weeks after removal of adenoids, which had caused ear trouble, and the total ablation of the healthiest tonsils one is likely to see. Might not the retention of the unoffending lymphoid tissue between the pillars of the fauces have acted as a sieve to restrain such a lethal invasion of the specific organism of anterior poliomyelitis? Surgeons do not scoop out normal lymph nodes of groin, axilla, or neck when a patient has an infection of toe, hand, or lip, unless there is present evidence of secondary infection of major importance. I fear that the tonsil may have also a protective function even if it be an atrium for invading microörganisms. Operators should remember that the vestibule door of a house keeps out sneak thieves, though it may occasionally admit an unwelcome guest.

The tonsils are not unnecessary organs, even if laryngologists do tell us they are; appendices are often valuable additions to books, and may be to the human animal. The suprarenal body, the carotid gland, the hypophysis, the thymus, the thyroid were recently organs of unrecognized activities. Their value to the economy is now established.

"Potential" Dangers

Potential dangers should not always lead us to take operative risks. Sometimes the etherizer, the trained nurse, the pathologist's microscope, the chemist's vial, the surgeon himself, or the contingent circumstances of the patient, the time, the place of

operation, or the "perversity of inanimate things," may be more dangerous than aberrant cells, the invading microörganism, or the neurotic crisis.

"Potential" is a word to scare patients, but not wise surgeons. Arsenic, strychnin, mercury, opium, and alcohol are potential poisons, but shall we fear them and never use their power? Must we throw them out of our armamentarium? A sharp knife in the hands of a clever cutter is potentially more dangerous than a doubting mind in the skull of a thoughtful surgeon, who believes that all problems cannot be solved by a keen edge alone.

Many fractures result in good function and good anatomical result without running the risk of ether poisoning, septic contamination, and amputation; some breast nodules are not the precursors of horrid death by malignant ulceration and invasion; some appendices remain anatomically valuable, perhaps physiologically so; an ovary may often look sclerosed to the ignorant eye without needing removal. Nature does not require the kidney of a biped vertebrate to be rigidly glued to his back bone; all pains in the lower right quadrant of the abdomen are not due to the vermiform appendix; spinal puncture may be more deadly than a doubtful injury to the cerebrum.

"Potential" malignity has caused the sacrifice of a good many female breasts; "potential" perforative appendicitis has led to unnecessary abdominal sections; "potential" tonsillar atria of infection have deprived many children of tonsils that were doing no harm.

Greatly would some of us have increased our operative lists had we stitched to the lumbar muscle all the loose kidneys referred to us for operation. How many so-called sclerosed ovaries were removed twenty years ago, during the bloody operative crusade against unrecognized neuroses, will never be known. The loss of wages, limbs, and even lives from the present furor for fixing with metal supports fractures of the extremities is hard to estimate.

The scientific mind must be a doubting one, but it must not be too conservative to novelty and progress. My thesis is that a surgeon should be open to conviction, but not carried away by

enthusiasm born of illogical hasty conclusions based on superficial study, half-understood physiological processes, and other unsafe premises.

It would be easy to relate case after case, in which a doubting attitude of the consultant or the better knowledge of the family physician has saved a family from the anxiety inseparable from operative attack on person and pocket-book, and perhaps preserved ovary, breast, limb, and even life.

Surgery must be regarded as a science, a part of all sciences, and not a mere art, if we who pose as surgical specialists wish to rank with the wise men of the earth.

To some of my hearers this paper may seem like a conservative cry that denotes a static surgical mind not receptive to the advances of a progressive science. I earnestly hope my doubting mind on some present-day problems may not be closed yet awhile to scientific enthusiasm and serious study.

I, however, freely admit my dubious mental attitude to dogmatists in surgery, science, and religion. They tire me and fill me with doubt. The Creator seems wiser than most authors of the latest fads in operative therapeusis. The human animal needs, as a rule, tonsils, vermiform appendix, mammary glands, aye, and his colon! Pathological deviations from normal in these and other organs may often be corrected by other methods than excision. A painful eye should not always be plucked out and cast from one. It is pleasanter and safer to wear correcting lenses. So also is it cheaper, pleasanter, and safer to drink water and take exercise than to drink wine and ride in an automobile and later have one's colon extirpated.

CERTAIN SYPHILITIC AFFECTIONS OF THE HEART AND AORTA*

By J. M. ANDERS, M.D., LL.D.

A variety of morbid states of the heart and bloodvessels, all serious in nature, may develop during an attack of unquestioned syphilis. While the writer would not go so far as to say with some recent investigators that syphilis is the principal factor in the production of heart disease, it can at least be safely assumed that rheumatism and syphilis head the list as causes of organic injury to this organ. The advent of the Wassermann reaction has shown in a convincing manner that the role of syphilis as an etiological factor in disease of the cardiovascular system had previously been underestimated. It is frequently the earliest clue to lues, especially in females, who, in many cases at least, know nothing of syphilitic infection, while in other instances a Wassermann reaction will, as has been well said, "unlock the tongue."

The cardiac lesions caused by the Spirocheta pallida are usually considered as belonging to the tertian stage of syphilis, but recent investigators have shown that they may develop soon after primary infection. Grassman[1] and later Brooks[2] and others have expressed the opinion that damage of a serious character may appear as early as the forepart of the second stage. The fact should not be lost sight of that both aortic and cardiac syphilis may be the result of hereditary lues. It is definitely known that the Spirocheta pallida has a selective action for the heart. As stated elsewhere, "of all the viscera the heart is among the earliest

* Read June 2, 1915.

to become involved in this disease." The importance of recognizing the cardiac element at the earliest possible moment is further shown by the fact that involvement of this organ may develop soon after the primary infection without symptoms which attract attention until months or even years later.

The claim made by Landois, Citron,[3] Hausmann, Sears,[4] and others that lues may affect the heart alone is both interesting and important. In two infants who died, one at three months of inanition, the other at eight days of asphyxia, Warthin and Snyder found the Spirocheta pallida in the heart muscle, while neither histological lesions nor spirochetes were found elsewhere.

Among the commonest cardiovascular conditions due to syphilis are myocarditis, aortic regurgitation, angina pectoris, and mesaortitis often resulting in aneurysm.

Mesaortitis. Since mesaortitis with or without coronary changes is commonly the primary complaint in cases in which, as frequently occurs, two or more of the affections named above are found in association, it will be considered first in this paper. That this condition is due in many cases at least to syphilis has been demonstrated, both by postmortem evidence and the results of carefully conducted therapeutic observations. In 1910 Longcope[5] pointed out that a peculiar type of arteriosclerosis (mesaortitis) was frequently associated with aortic incompetency, due to chronic aortic endocarditis. For example, in a series of 37 autopsies showing mesaortitis a chronic aortic endocarditis occurred thirteen times, or in 35.1 per cent. Again, in 21 cases of chronic aortic endocarditis unassociated with lesions of any other valves occurring in connection with mesaortitis it was found that the lesions varied somewhat in extent in the individual instances, "but were always confined, and often sharply localized, to the arch of the aorta."

Of the 21 cases of aortic insufficiency associated with mesaortitis, 11 gave a definite history of either syphilitic infection or syphilitic lesion (gummata).

Harlow Brooks,[6] who made an anatomical study of the heart and aorta in 50 consecutive autopsies, found that 66 per cent., "in-

cluding well and incompletely treated instances, died as a result of, or with serious circulatory disease apparently of specific origin." Of these the myocardium was seriously involved in 44 cases, the coronaries in relatively greater degree than the general arterial system.

That this mesaortitis is of specific nature with definite characteristics is shown by the fact that the spirochetes have been found by Schmol and Wright in the lesions, the latter being able to demonstrate these organisms, often in enormous numbers, in all of 5 cases. Says Osler: "Microscopically the most important changes are found in the media and adventitia: (*a*) perivascular infiltration of the vasa vasorum; (*b*) small-celled infiltration in areas of the media, with (*c*) splitting, separation, and destruction of elastic fibers and the muscle cells. The process is largely a productive mesaortitis, and so marked may be the foci in the adventitia and media that they look like miliary gummata, and, in fact, were so described as far back as 1877 by Laveran and by Heiberg."

Aneurysm. The intimate connection between lues and aneurysm was well known to the older writers—to Pari, Larcisi, and Morgagni—but it has been especially emphasized by many modern writers, among whom the names of Osler, Heller, Koster, Chiari, Benda, and Klotz are conspicuous.

The belief that in persons under forty-five years of age, syphilis plays the overshadowing role as an essential factor in causing aneurysm is confirmed by practically all of the more recent writers. On the other hand, it may not be wholly gratuitous to caution the medical profession, as Hausmann has done, against regarding every case of aneurysm, even in syphilitic subjects, as due to lues.

Two additional facts may aid materially in distinguishing the etiological variety of aneurysm under discussion, namely, that the root of the aorta, *i. e.*, the ascending portion of the arch, is the usual seat of luetic aneurysms, and that they are frequently multiple.

Statistical evidence is not wanting to strengthen the view that

syphilis is the most potent etiological factor in the production of aortic aneurysm. Cumston[7] quotes Rasch, of Copenhagen, who found 28 aortic aneurysms in a series of 3165 autopsies. In 16 cases syphilis was positively known to exist, or 57 per cent., while in 7 others, that is, 25 per cent., syphilis could be taken for granted in all probability. Etienne in a total of 240 cases of aneurysm found syphilis to be the cause in 166 cases, or 60 per cent. These figures have been amply confirmed by the following among other percentages: Malmsten, 80; Heller, 85; Hampeln, 82; Pansini, 65.

My own collective investigations yielded a totality of 621 cases, of which number 363, or 58.5 per cent., were of luetic origin. In view of the fact that some of these cases had not been submitted to the Wassermann test, this percentage is too low. Among 8 instances included in the above figures occurring in the Medico-Chirurgical Hospital 6 were caused by lues.

A full discussion of the diagnosis of syphilitic thoracic aneurysm is not within the scope of this paper, but I desire to lay particular stress on a single fact bearing on this phase of the subject, namely, that a positive Wassermann reaction without confirmatory historical or clinical evidence (*e. g.*, age of the patient, site of the tumor-like protrusion, history of specific infection, etc.) does not warrant an assured diagnosis of lues.

Aortic Incompetency. Syphilis is now generally regarded as an essential factor in the causation of aortic incompetency, more particularly in cases which develop before the forty-fifth year of life. The chronic aortic endocarditis is commonly associated with mesaortitis, as before stated, affecting the root of the aorta, and indeed may be the result of direct involvement of the segments in such cases. It is worthy of note that this etiological variety of aortic incompetency is often met with, unassociated with wide-spread arteriosclerotic changes. In this connection it should be stated that a pure mitral lesion is seldom produced by lues, but a combined aortic and mitral is commonly caused by syphilis.

There is a consensus of opinion to the effect that the most important etiological factor in the production of aortic incompetency is luetic infection. This view is amply supported by sta-

tistical observations. Thus Longcope[8] in a series of 37 autopsies showing mesaortitis found 13 instances of chronic aortic endocarditis (35.1 per cent.). Again, of 21 cases of aortic insufficiency, 11 either gave a definite history of syphilis or syphilitic lesions were discovered at autopsy. Citron obtained a positive Wassermann reaction in 10 out of 16 cases of this cardiac lesion, or in 62.6 per cent. Fiessenger[9] obtained a history of syphilis in 28 out of 37 cases of aortic insufficiency. Collins and Sachs[10] found a positive Wassermann reaction in 10 out of 13 instances of aortic valvular disease. Babcock[11] records 16 cases of aortic regurgitation of which 11 were submitted to a Wassermann test, with a positive reaction in all of the cases.

My own collective investigations into the question of the frequent association of aortic insufficiency and syphilis embrace a total of 219 cases, inclusive of the figures cited above. Of these, 133, or 60.7 per cent., were clearly due to lues. In a considerable number of the cases of aortic incompetency no reference to the Wassermann test was noted. Obviously, then, the above figures underestimate the true role of syphilis in the production of this condition.

Severe pains may attend an invasion of the valve segments often accompanied by angina pectoris from implication of the coronaries in early cases developing more or less acutely. If the specific character of the cause be overlooked, an inappropriate or the usual routine treatment of chronic valvulitis be adopted, these cases may reach an early fatal termination. On the other hand, intensive antisyphilitic treatment may, if instituted early, bring about marked improvement and the cases progress as aortic incompetency due to other causes.

While a certain diagnosis of syphilitic valvulitis affecting the aortic segments cannot be made without a clear history of either specific infection, or a positive Wassermann reaction, supported by confirmatory evidence, yet in the absence of rheumatism, gout, lead, alcoholism, pyogenic infection, or a predisposing occupation such cases should be labeled suspects and given the benefit of vigorous antisyphilitic treatment. Obviously, in instances

belonging to this group the Wassermann test should be carried out whenever possible, before remedial measures are instituted.

There are a few special physical signs which aid in the establishment of the luetic character of the chronic valvulitis. For example, Sachs[12] points out that "enlargement of the left ventricle is generally not so marked as in other forms of aortic insufficiency, and therefore the capillary pulse and double sound over the crurales are not so marked." I have observed the presence of a more decided arrhythmia in cases of aortic incompetency due to syphilis than in those due to other causes.

The early recognition of the true nature of the lesion becomes a matter of much practical importance to the end that the ravages of this disease may be, to a great extent at least, obviated by suitable treatment. In this connection it should be pointed out that congenital cases of this affection may be due to hereditary lues.

In cases in which the history is obscure, too much stress cannot be placed on the value of the Wassermann reaction as a means by which to determine the etiological variety in question. As in the case of aneurysm, so in aortic incompetency, a positive reaction alone unsupported by other clinical evidence does not warrant an assured diagnosis of lues, but it renders it highly probable that syphilis exists.

On the other hand, it must be recollected that aortic incompetency occurring in a luetic subject may be due to causes other than syphilis, more especially if the valvular lesion develop after middle life. Here it should be noted that the cardiac lesions of syphilis usually appear within two or three years after infection, a fact of considerable diagnostic significance, in some cases at least.

Myocarditis. As stated before, early involvement of the myocardium is not infrequent in the course of syphilis. Isaac Adler[13] first pointed out that the most important lesion of the heart is one of the myocardium, which lesion is dependent on periarteritis of the coronary vessels. Here it should be well understood that while endarteritis is the frequent important lesion, actual

gummata in the myocardium are distinctly infrequent. Warthin[14] has described a syphilitic interstitial myocarditis in the absence of coronary periarteritis, and has demonstrated that the light-staining patches of proliferating stroma represent localized colonies of the spirochetes. Mareck, Simons, Buschke, and Fischer have also demonstrated the spirochetes in the diseased muscle of luetic myocarditis.

The recognition of incipient myocardial involvement is difficult since the functional derangements thus produced are often slight, or, indeed, the condition may be entirely latent. The onset of the symptoms, if it develop in the secondary stage of syphilis may be somewhat rapid or even acute. The principal features are arrhythmia, particularly intermittence and tachycardia, and less commonly extrasystoles. Brooks emphasizes, among the earliest symptoms, "irregularity of action, more marked when strain is added by mild exercises or through nervous apprehension." He found the same thing true of the tachycardia, which is "incited to a degree by conditions which in the normal would fail to elicit such a response." Grassman writes: "I have studied 288 cases of secondary syphilis, and in 85 per cent. found disturbances of the rate and rhythm of the pulse, while in 40 per cent. accidental murmurs, usually with dilatation, occurred."

Pain is not, as a rule, a prominent feature in the early phases of the disease, although a feeling of thoracic oppression and slight dyspnea may be noted. In rare instances, in which extensive lesions are present, actual pain with more or less tendency to radiation may be observed. The symptoms enumerated do not differ from those due to the myocarditis of other infections than syphilis, and it has been shown that these indications may all disappear in the course of a few days as the result of energetic antisyphilitic treatment—a fact that emphasizes the importance of an early recognition of the condition.

In the tertian and quartenary stages of myocardial syphilis the symptoms and signs do not differ materially from those presented by myocarditis due to other causes. Not a few cases are latent and unsuspected during life, but are discovered if they

come to autopsy. Soon or late, in some cases, dilatation is observed to occur, especially as the result of unwonted exercise, and this may be attended with a murmur.

Anginoid pains are not uncommonly present and obliterative endarteritis implicating the coronaries and producing myocarditis, may result in attacks of true angina pectoris.

The markedly irregular character of the arrhythmia has been, as stated above, emphasized by Brooks, and his observation has been confirmed by my own experience. The observation first made by Runeberg, namely, tonelessness of the first sound at the apex, has since been confirmed by Callender[15] and others.

It is to be observed that neither a characteristic grouping of features nor a single pathognomonic symptom, unless it be a positive Wassermann reaction, are presented by the condition. As regards the Wassermann test, it may be said that although a positive or negative reaction is not an absolute criterion of the presence or absence of a syphilitic infection, Brooks contends that it is better than the 70 per cent. of error, based on the history or clinical findings alone.

Certain clinical peculiarities already mentioned may, however, serve to arouse suspicion of syphilis. Of these, the tonelessness of the first heart sound, and the decidedly irregular, accentuated character of the arrhythmia deserve special mention. Again, the association of phenomena which point to syphilitic involvement of other organs and structures of the body often throws light on the character of any cardiac lesion that may be present. Lastly, all determining causes of myocardial disease other than syphilis should be carefully excluded.

Heart-block is frequently caused by syphilitic lesions of the bundle of His, but this phase of cardiac lues cannot be enlarged upon here. Suffice it to cite the figures of Robinson, who found that among 16 cases of heart-block due to such lesions, 6 at least were of syphilitic origin.

Angina Pectoris. The writer has collected 270 cases of angina pectoris from the literature, of which only 72, or 26.5 per cent., gave evidence of syphilis. This percentage, however, is

much too low, since in 250 of the recorded instances no mention was made of a Wassermann test, sole dependence being placed in the history. The close association of syphilis and angina is amply confirmed by modern authorities. Breitmann[16] of St. Petersburg, writes: "Every case of angina pectoris during the younger period of life is open to the suspicion of syphilitic origin. R. O. Moon[17] has been much impressed with the great predominance of lues in connection with true angina, and has seldom met with a case since the advent of the Wassermann test which did not give a positive reaction. Saundby[18] states that congenital syphilis as a cause of angina pectoris is not to be overlooked in young patients.

Prophylaxis. My discussion of the treatment of cardiovascular syphilis will be, owing to the exigencies of time and space, limited to prophylaxis. Doubtless, the incidence of cardiovascular disease would be much lessened by a more systematic and vigorous treatment of luetic infection in general. There is perfect unanimity among syphilographers and clinicians of wide experience regarding the belief that when either syphilis of the myocardium of marked extent or aortic incompetency exists a cure is impossible of attainment.

Physicians should therefore feel themselves charged with a serious responsibility on behalf of the victims of luetic infection, and carry out the treatment of early syphilis in the wisest manner possible. An added reason for adopting this course lies in the hazard arising from the administration of salvarsan or neosalvarsan in the severer forms of cardiovascular syphilis. It has been found that death, either occurring suddenly or after several days from the use of these agents, is commonly due to myocardial degeneration, secondary to coronary lesions.

As stated elsewhere, "a sane view of the prophylaxis of cardiac involvement in this disease demands inclusion of the treatment of its secondary manifestations." It is in this stage that its development may take place, and also that the time of cardiac invasion can be fixed, by the appearance of certain clinical features, in some cases at least.

In concluding, the writer desires to make grateful acknowledgment of the assistance rendered by Drs. H. Leon Jameson and Andrew A. Anders in the work of searching the literature in connection with these statistical investigations.

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DISCUSSION

Dr. George W. Norris: Dr. Anders's very able and apt paper on the subject of syphilis in relation to disease of the heart in which he called our attention to the prevalence of syphilis in association with heart disease and summarized a good deal of the recent literature in a very interesting way, must have appealed to us all.

The subject brings up a number of interesting thoughts. One is that of Oliver Wendell Holmes's remarks about Ricord, whom he referred to as the Voltaire of pelvic literature, a skeptic as to the morality of the human race in general, who would have submitted Diana herself to a treatment with his mineral springs and ordered a course of blue pills to the vestal virgins.

There can be no doubt, as Dr. Anders has told us, that since the discovery of the spirochetes, and since the Wassermann reaction has become known to us, we have learned to recognize a number of lesions as definitely syphilitic which in the past we barely suspected to be such. In this relation it is interesting to note the way in which experimental medicine sometimes follows empirical medicine. It had long been known by practitioners that the iodides did good, as did also, in a good many of these cases, small doses of mercurials. We do not know the way in which the

iodides do good because we do not know the way in which they act; it is assumed that it is by the action of a proteolytic ferment upon granulomatous tissue. It is interesting to bear in mind that the iodides often fail unless they are combined with mercury. According to the modern method of treatment we not only use both of these drugs but frequently salvarsan in addition.

In the last year more attention has been given to syphilitic nephritis and it is somewhat comforting to know that if we do give mercury or salvarsan to these patients we are rather apt to benefit their nephritis rather than injure the kidneys by these otherwise irritating drugs which we may administer. One of the points which, although not particularly emphasized by my own personal experience has, I think, been more or less emphasized in the literature, is the frequency with which sudden death may occur in these cases of syphilitic myocarditis, not only among the old but among the young. Among the symptoms which have struck me as having some diagnostic value in syphilitic myocarditis are low blood-pressure, mild angeoid attacks associated with dilatation of the left ventricle and as Dr. Anders has emphasized, cardiac irregularity followed by auricular fibrillation. In these cases it is well to remember that salvarsan must not be administered without due consideration. We know that salvarsan is not an altogether innocuous drug and does have a tendency to lower blood-pressure.

Another point in which I was interested, and which I was glad to hear Dr. Anders bring out, was the question of syphilitic aortitis even in the young. It has been shown that a considerable percentage of newborn infants who die shortly after birth can be shown to have spirochetic disease in their aorta.

Gumma of the heart can be rarely diagnosticated during life because it often involves the silent regions of the heart; a presumptive diagnosis may, however, be made if the gumma involves the conducting system of the heart and in which we find a heart-block.

Regarding the question of treatment, I realize that Dr. Anders could not in the time available attempt to discuss that, but he did ask for an earlier treatment of these cases. Cases of syphilis are inadequately treated in our dispensaries. Some of the hospitals in this city have refused, or do not like to treat syphilis in its early stages, and will not admit secondary lues to their wards. Sometimes there seems to be a general attitude among the boards of managers in hospitals that it is the patient's own fault and they can stand the consequences. They are perfectly willing, however, when the patients come back with the disease at a practically incurable stage to admit them. It seems to me that the more efficient and thorough treatment of syphilis in dispensaries is one of the crying needs of our medical work today.

After all there is much truth in the dictum of Charcot who said that if we knew syphilis and tuberculosis in all of their manifold manifestations we knew a large part of medicine.

Dr. James Tyson: Dr. Anders's paper and Dr. Norris's discussion recall vividly my own experience as a young man in dispensary service and our method of treating cases which included rheumatoid affections. It was our practice to give first iodide of potassium. Failing with the iodide we added mercurial bichloride and it is astonishing what a large number of cases were at once benefited upon the addition of the mercury. It would seem, therefore, that the new methods confirm the older. Later observations and the demonstration of the syphilitic organisms are proving what the therapeutic test so many years ago also showed; and, I have sometimes thought that although this was a rough-and-ready method of treating symptoms, we perhaps might adhere to it with advantage a little more frequently than we do in modern times.

Dr. Anders (closing): I was glad to hear Dr. Norris say that we could employ salvarsan and mercury in cases of nephritis due to syphilis. I have seen several very remarkable results in such instances from the alternate use and also from the separate use of these two agents. On the other hand, we must be very certain in these cases that syphilis is the real cause of the cardiovascular and renal conditions. Only lately I saw very disastrous results follow the administration of mercury in a case of nephritis which had been misdiagnosed as being of syphilitic origin, the patient dying in a few days, when otherwise he might have lived for months or even for years. Mercury has its selective affinity for the kidneys and there is no other variety of nephritis than the syphilitic in which we are justified in employing it.

While it is true that since the discovery of the Wassermann reaction the true importance of syphilis as a factor in many heart diseases has been in great part established, this cannot be said of this test in relation to angina pectoris. The close association of angina pectoris and syphilis therefore remains to be established, according to my figures, at all events, but I verily believe it will be, once the profession is alive to the importance of making Wassermann tests in all cases of angina pectoris. During the early stages of syphilis we should carefully examine the heart systematically. I am confident that neglect of this precaution is attended with untoward results in many cases. We now know that in one-half at least of these early cases, certain symptoms (mentioned in my paper) arise which should arouse suspicion of cardiac involvement and lead to the most vigorous antisyphilitic treatment. Truly, with regard to cardiac involvement in the course of syphilis, the words of John Locke apply: "Prevention is better than cure, and far cheaper."

SOME APPLICATIONS OF PHYSICAL CHEMISTRY TO PROBLEMS IN MEDICINE[1]

By HENRY LEFFMANN

Half a century ago scientists were wont to divide the forms of natural energy—termed forces—into two classes: the physical forces, such as light, heat, and electricity, which act apparently at unlimited distance, and the molecular forces, cohesion, adhesion, and chemical affinity, which act at insensible distances. The last was the special province of the chemist, and the phenomena due to it were presented in great variety. The other two were given but passing notice. The study of their actions was commonly classed as "chemical physics," and though not widely cultivated, regarded as an inviting field of research.

Much change has come over the spirit of the dream in the last quarter-century. Under the title "Physical Chemistry" a vast and intricate science of molecular conditions and transformations has grown up, and has begun to throw light in many directions upon the problems presented by both living and non-living matter. All progress seems to tend to draw together all classes of phenomena and to show that

"All are but parts of one stupendous whole."

It is my purpose and hope to set forth in this paper, in a plain manner, a few of the data of physical chemistry that bear directly upon practical medicine. The science is abstruse and the facts can only be treated in an elementary way.

Out of the vast array of data that have been elucidated by earnest

[1] Read October 6, 1915.

workers in all civilized lands, I select for the purposes of this paper two phenomena, the terms for which, familar to chemists as household words, are but little known to those in general medical practice. These phenomena are "ionization" and the "colloidal state." I must admit that both terms are, like the terms evolution and environment, much overworked, but we cannot doubt that the conditions indicated by them are of profound significance in physiology and pathology, though at present the data are but few in proportion to the scope of the study. We may, I think, prophesy that great as is the literature of these subjects, it is but the baby figure of the giant mass of things to come.

The phenomena of ionization are concerned especially with the condition ordinarily called solution, the latter term being here limited to fluids produced by association of substances, one of which is primarily a liquid. The term solution has a much wider significance in physical chemistry—common glass being considered a solution—but I will not apply this broad meaning in this paper.

When we dissolve common sugar and common salt in water we designate the liquids so obtained "solutions." Most persons would consider them of the same general nature, and they were so considered by all physicists and chemists until a few decades ago. It is now known, however, that the salt in dissolving has undergone a very important modification, by which its activity has been materially increased, while the sugar has suffered no such change. The salt contains two distinct forms of matter, the sugar three. The elements of sugar are supposed to remain in essentially the same association as when undissolved, but the elements in the salt have been in a certain way loosed from each other and have assumed electrical charges. To present the concrete statement, sodium atoms of the salt have by the act of solution acquired a positive electrical charge, while the chlorin atoms have acquired a negative charge. The proportion of the salt thus modified is dependent largely upon the mass of water present. If the solution is concentrated, a considerable proportion of salt remains unchanged; if dilute, a considerable proportion becomes changed. The modification of a substance by which it acquires these electrical charges

is termed ionization; the respective positively and negatively charged elements are termed "ions." The importance of the change lies in the fact that the chemical activity of the substance and the pressure of the solution are much enhanced by it. It is found that the most potent ionizing liquid is water, and that solutions of a given substance in alcohol, ether, glycerol, or acetic acid are not equivalent to a water solution nor to each other. Generally, the degree of ionization is increased by dilution. Interesting explanations of well-known phenomena are now possible under these principles. Boric acid is of the same type as nitric acid, yet is far less active. The difference is due to the fact that boric acid is but feebly ionized, while nitric acid is largely ionized. Concentrated acetic and concentrated sulphuric acids are very corrosive; the latter even when much diluted is intensely sour and very active; the former when much diluted is a widely used condiment. The difference is due to the fact that acetic acid ionizes to but a limited extent.

A striking example of the influence of ionization was developed in researches of Paul and Krönig.[1] It is well known that most mercuric compounds are poisonous, and in view of the similar qualities of cyanids, it would naturally be inferred that mercuric cyanid will be extremely toxic. As a matter of fact, it ionizes so feebly that it is not capable of conducting appreciably a current of electricity, or of yielding the ordinary reactions of mercuric salt, and Paul and Krönig found that its germicidal action on anthrax spores is almost *nil* as compared with mercuric chlorid and bromid.

The problem of ionization is comparatively simple when such compounds as sodium chlorid and potassium cyanid are considered, for these contain the respective ions in unit amounts, and but one division is possible. With complicated bodies the division may occur by more than one line and a long series of painstaking researches will be needed before the laws governing this class of phenomena will be made out.

The application of the data of ionization to the interpretation of

[1] Quoted by Philip, Physical Chemistry, 163; and Ostwald, Foundations of Analytic Chemistry, 181.

the action of medicines is complicated by the fact that living protoplasm and membranes have specific selective powers, and thus tests *in vitro* may mislead. An example of this is found among the mercuric salts. Under given conditions mercuric nitrate ionizes to a much greater extent than mercuric chlorid, yet the latter is ordinarily more toxic. According to Höber[1] this is due to the fact that the chlorid is more soluble in the lipoid substances contained in the membranes, and thus is enabled to get into contact with the protoplasm of the cells. It has also been found as a corollary of what has just been stated in regard to the inactivity of mercuric cyanid, that a mixture of mercuric chlorid and hydrocyanic acid is more toxic than an equivalent amount of mercuric cyanid, as the former substances ionize to a marked degree.

Another important point is the influence of salts upon one another. It might be supposed, and indeed, has long been supposed, that when a mixture of two or more substances shows no appreciable change of condition, such mixture will have the properties of all the ingredients, but this is far from being generally true. It would lead me too far into the recondite fields of physical chemistry to discuss the reason for this, but I may present a few instances. One has, indeed, just been mentioned. A mixture of mercuric chlorid and hydrocyanic acid is not equivalent to mercuric cyanid, not merely because of the presence of hydrogen and chlorin in the respective compounds, but because the substances react in a different manner to the dissolving liquid. Inasmuch, however, as other solvents than water act but feebly in ionizing, it is not unlikely that an alcoholic solution of mercuric chlorid and hydrocyanic acid would have a closer equivalency to mercuric cyanid than a solution in water.

The cyanids afford several striking instances of the anomalous effects of mixtures. The common soluble forms, such as potassium cyanid, are extremely active poisons, but when they are associated with iron cyanids in certain proportions, which are themselves poisonous, a comparatively innocuous compound, potassium ferrocyanid, is formed.

[1] Philip, loc. cit., 165.

What do these data suggest in regard to the use of drugs? I think they point to the importance of simplification in prescriptions. Present-day physicians have freed themselves to a great extent from the so-called "shotgun" combinations of olden time, but by no means as thoroughly as ought to be. The files of any drug store will show most extraordinary mixtures, violating not merely the principles briefly indicated above, but the simple and widely known principles of pharmaceutical chemistry. I recall a prescription described to me by a druggist in which two preparations were directed to be carefully detannated, and then a third, rich in tannin, was given, added without any comment. I have known antikamnia, ammonol, and acetanilid to be ordered together. This was in earlier years when both these proprietaries contained acetanilid.

It will be said that it is often required to give two or more substances in the same course of treatment. How is this requirement to be met? In the first place, the simpler principles of incompatibility are widely known and may be applied. In the second place, the constant endeavor of the prescriber should be fewness of ingredients. When in doubt, leave out the substance or administer it separately. Many years ago I was much impressed with the answer made by a prominent member of the homeopathic profession of this city, who, as a witness in a murder trial, was, at my suggestion, asked by the prosecuting attorney what he would consider the therapeutic value of a certain mixture of a few common drugs. He replied that the principles of the school of practice which he followed did not permit of associating two potent substances in one dosage. The method is to administer the several drugs at intervals, so that one may have entered the system and produced its action before the other is exhibited. May not this procedure be commended to the consideration of practitioners of the regular school, especially in view of the vogue of tablet, pill, and capsule?

The phenomena of reaction of salts to the solvent and to each other when associated in solution have important applications to the so-called "mineral waters," several types of which are in extended use. In most cases the ingredient for which the water is recommended is present in small proportion and associated with

many other substances of more or less physiological significance. No class of waters shows more untrustworthiness in these respects than the so-called "lithia waters." Many thousands of gallons of these are annually consumed with the object of getting the solvent action of lithium salts upon uric acid. Analysis of these waters shows that in most instances the lithium is infinitesimal in amount, and that in the few that contain appreciable proportions, so much of other salts is present as to confuse the therapeutic values. Moreover, the exhaustive investigation made a few years ago by Haywood and Smith for the United States Government indicates that the lithium is generally present as lithium chlorid, not carbonate, which latter is the salt that Garrod used in the experiments upon which he based his theory of lithium treatment. The data of physical chemistry would lead us to the view that if a water contains a substance that renders uric acid soluble and also one that renders it insoluble, the latter would be the active substance, and the water would be of no advantage as a corrective of uric acid deposit. In the report of Haywood and Smith, three well-known American waters are given as containing enormous proportions of sodium, calcium, and magnesium salts in comparison with the lithium. It is obvious that one cannot expect to get solely the action of lithium by administering such waters.

A side light upon the possible actions of the salts commonly found in mineral waters is thrown by the researches published by Loeb.[1] Experiments were made with the larvæ of a species of barnacle. If the freshly hatched individuals are placed in a solution containing sodium chlorid, potassium chlorid, and calcium chlorid of the concentration and proportion of sea-water, most of them will go to the bottom of the tank. If the proportion of calcium chlorid is increased the larvæ will swim as they do in normal sea-water.

Similarly, it has been found by agricultural chemists that magnesium compounds in the soil have an unfavorable action upon many plants, but that addition of calcium compounds often rectifies this. Here we see evidence that a substance may act favorably by

[1] Proc. Nat. Acad. Sci., 1915, i, 459.

reason of its specific antagonism to another, a sort of physiological antidote.

Another point that has been brought into prominence by the progress of physical chemistry is the influence of fine division, especially extremely fine division. A new department of research—ultramicroscopy—has been developed of late years, dealing with the methods of rendering visible particles quite undetectable by ordinary microscopes. Let me discuss briefly and in an elementary manner one point in this phase.

If we imagine a cube with a side of one inch, the surface will be six square inches. If we divide it into two equal parts each part will have an area of four inches, that is, the surface has been increased 50 per cent. It is obvious that as the division proceeds the total area will steadily increase, and when the particles become very small the surface area will be enormous. According to Zsigmondy and Siendentopf some fine divisions of gold consist of spheres having an average radius of 0.00001 mm. A sphere of radius of 1 mm. if divided into spheres of 0.00001 mm. radies will have a total surface of 100 square meters. It follows from such a consideration that by dividing a material finely we greatly increase the facility of chemical action. We also confer other qualities among which are constant self-agitation and easier passage through porous partitions. Many years ago the botanist Robert Brown observed the behavior of minute particles suspended in a liquid which has been called the Brownian movement. Everyone knows that if we powder a substance finely we can increase the rapidity of its solution, and if not soluble we can increase the duration of its suspension.

The common emulsions illustrate this principle, though their preparation generally involves other physical principles. Other things being equal, the finer the powder, the longer it will remain suspended. This is the basis of the procedure termed elutriation, employed in the manufacture of prepared chalk, calomel, and bismuth subnitrate.

It follows from these considerations that medicines that are insoluble or difficultly soluble in the fluids of the body should be

administered in as fine powder as possible, and here again we have to give reason to the homeopathic school, for their repeated triturations must in a measure potentize such substances as arsenic, calomel, bismuth subnitrate, and many resins and proteins.

Manufacturing pharmacists do not always apply the highest principles of physical chemistry in their processes, and hence we sometimes find in drug stores preparations of distinctly inferior quality. Some years ago I had occasion to investigate a case of suspected poisoning in an infant to whom, among other drugs, several large doses of bismuth subnitrate had been given. No poison was found, but a notable quantity of the bismuth compound remained in the stomach. On examining it with the microscope it was found to be made up largely of comparatively large crystals, evidently an unsatisfactory form for administration of so insoluble a substance. I was led to examine a number of samples, and found that three sources of supply were used by most Philadelphia druggists, two of them local makers and one a French preparation. The last named was an almost impalpable powder, the other two crystalline, one of these much coarser than the other. It is plain that whatever effect bismuth subnitrate has will be most quickly obtained by the use of the foreign article.

The physical chemistry of colloids is now occupying a vast army of workers; the literature is growing with great rapidity. The topic boasts at least one journal exclusively devoted to it. The initiative in this field is due largely to an English chemist, Thomas Graham, who, in 1861, published the results of experiments on diffusion through membranes, finding that when a mixture was made of two substances, one of which was crystallizable and the other not, the former would pass rapidly through the membrane while the other would be held back. He divided substances into two classes, "crystalloids" and "colloids." A solution of gelatin and common salt in water exemplifies both types.

At the present time the terms "colloid" and "colloidal" are given much wider significance than Graham intended. This is to some extent to be regretted, but seemingly cannot be helped.

It will be quite impossible to give here, even in outline, the present status of colloid chemistry, but I want to present a thought that

has come to me lately which I think is worthy of consideration. It is now known that a classification of substances into crystalloid and colloid is not fundamental. These are conditions only, and the same substance may assume both states. The crystalline condition probably results when molecular attractions are allowed more opportunity of acting: the colloidal condition results when less opportunity is offered. Hence we find, as an almost universal rule, that if we allow time for a substance to solidify from a liquid or gaseous state crystals are produced, and these are the more distinct and perfect as the time of separation is prolonged. If the substance is solidified rapidly an amorphous (colloidal) mass is produced.

It is also found that the presence of a minute amount of a crystal of the substance in solution will materially promote the separation in crystalline form, acting as a nucleus for the operation of the molecular forces. The action of such a nucleus is especially shown when the solution is near the crystallizing point. Now it has long been known that many substances can be held under special conditions in notable excess of that held usually. Such solutions are termed "supersaturated," and they are, as a rule, very unstable, tending to deposit the excess under slight disturbance.

Most of the ingredients in normal human urine are more soluble in hot than in cold water, and among these is uric acid which is but slightly soluble at any temperature. Although modern pathology does not give to this substance nearly so large a share in producing the ills that flesh is heir to as did older medicine, yet it is a factor to be held always in view. There is no doubt that whatever may be its effect when in the blood or deposited in the tissues, it is a serious interference when separated in the crystalline form from the urine. The old notion that its production is almost wholly dependent on a meat diet is now disproved, but some experiments lately made under the supervision of Dr. Martha Tracy, at the Woman's Medical College of Pennsylvania, indicate that a full meat diet increases the acidity of the urine. If this is established it will be an important point, for the principal danger from uric acid is in its separation in the crystalline form in some part of the genito-urinary tract. Such separation is promoted by increased

acidity, and if a minute crystal is deposited at any point it will act as a nucleus and bring about further separation, not only of uric acid, but of other compounds held in unstable solution in the urine. The common method of preventing this separation is by administering alkalies, especially lithium carbonate, but this may lead to the precipitation of substances such as phosphates, not soluble in alkaline urine, which would be no therapeutic gain. We see, therefore, how a full meat diet may cause or aggravate uric acid troubles, although not increasing the output of the acid itself.

Knowledge of the nature and properties of colloids enables us to explain many physiological and pathological phenomena. Colloids possess powers of attraction governed by different laws than either those of true chemical affinity or of ordinary adhesion. One of the suggestions of medical interest relates to the manner in which ferric hydroxid acts as an antidote to arsenic. It is well known that to secure this action the material must be freshly prepared. It is a colloidal mass. It acts probably by drawing to itself and holding the arsenic that has been dissolved in the fluids of the stomach and is about to pass into the circulating fluids of the body. In the same manner, aluminum hydroxid withdraws many organic substances from solution in water. This property of colloids is termed "adsorption."

Intimately connected with this field of chemistry is the subject of enzymes. These are probably the connecting link of living with non-living matter. They show colloidal properties, passing very slowly or not at all through parchment paper, and possessing high powers of adsorption, which is one of the reasons that they are difficult to prepare in the pure state. Chittenden pointed out that with some enzymes, *e. g.*, pepsin, the purer the material, the more sensitive it is to interference with other substances. The constituents of protoplasm are mostly colloidal, and the mineral substances in the fluids of cells are mostly ionized, so that the problem of the cell is largely a problem of physical chemistry.

I have, I presume, said enough to show that physical chemistry may be characterized by the description of politics which Mr. Pickwick gave to Count Smaltork: "A difficult study of no inconsiderable magnitude."

DISCUSSION

Dr. S. Solis Cohen: Dr. Leffmann's paper deals with a subject of such magnitude that a certain degree of temerity is required on the part of him who would approach it, not being a professional chemist. Clinicians and pathologists, while they realize the great significance of this subject must hesitate to put forward more than tentative opinions concerning any of the great problems into which physical chemistry enters; if for no other reason, for lack of knowledge concerning the great distinguishing factor between the test-tube reactions and the reactions that occur in the living body. As Maxwell has pointed out, there are certain problems that we are compelled to consider in the light of analogy, and yet the analogy is only partial and our conclusions must be qualified accordingly. In so far as the physicochemical reactions in the living body are the same as those of the laboratory, we may apply the laboratory findings to the problems of biology—to physiology, to pathology, and to therapeutics. But as regards the great and increasing number of the outstanding biological problems of the day, the value of unknown factor, the x, or the x, y, z, is so great, that we must hesitate. I think no stronger illustration of that can be given than the researches of Fischer upon edema and nephritis. These are perhaps to be reckoned among the most accurate, painstaking and comprehensive studies of recent years concerning the application of colloidal reactions in pathology; and yet I do not know any clinician or any pathologist who is willing to accept without considerable reserve, Fischer's far-reaching conclusions. It may be well to recall some of these in brief outline.

We must first recognize that the living tissue is—apart from its "living" characteristics—virtually a complex solid colloid or "gel," and that most of the fluids it produces are liquid colloids or "sols." Reduced to the simplest terms, the tissues and fluids involved in the production of the urine may be regarded as a physicochemical "system" of three "phases": two liquids—the blood and the urine—separated by a solid—the kidney tissue.

Disregarding its cells, the blood is a complex liquid colloid or "sol" normally neutral in reaction and containing a number of crystalloids—salts and non-electrolytes.

The "urinary membrane" or "kidney wall," including all the structures that separate the blood and urine, is a complex of various emulsion colloids in the solid or "gel" state, and containing also various electrolytes and non-electrolytes.

The normal urine is an aqueous solution of various crystalloids, electrolytes and non-electrolytes, derived from the blood, together with a very

small quantity of colloidal material, the so-called normal albumin and a variable quantity of mucin, etc., from the urinary tract.

Under pathological conditions the colloidal content of the urine rises, and we say that albuminuria exists; the tendency among pathologists hitherto being to regard this albumin as blood-serum which has passed through the urinary membrane, owing to the morbid alteration of the latter. Fischer, however, contends that it is derived from the solid protein colloids of the kidney wall, which have gone into solution in the urine.

He has shown that protein "gels" will not dissolve in the ordinary solutions of neutral salts, but that in either acid or alkaline solutions, up to certain limits of concentration, they will first swell excessively through the imbibition of water, and finally dissolve.

This tendency, however, is decreased by the addition of any neutral salt, and the inhibition is greater, the more concentrated the solution. Moreover, some ions act more powerfully than others.

Applying the result of these test-tube experiments to pathological conditions in the living body, Fischer asserts that the cause of nephritis and albuminuria is primarily an excessive acidity in the kidney blood, causing swelling and solution of the colloids of the organ, and that this with its concomitant interference with function may be inhibited in two ways: (1) by the introduction of alkali in sufficient quantity to restore the normal reaction; (2) by the introduction of solutions of potassium or sodium salts in greater concentration than that normal in the blood-serum.

Fischer therefore advocates the treatment of albuminuria and of edema resulting from nephritis, by the introduction into the blood, either directly or through the stomach, rectum or subcutaneous tissues, of a concentrated (*i. e.*, a hyperhematonic) alkaline saline solution; and suggests one containing from 10 to 20 grams of crystallized sodium carbonate, and 10 to 30 grams of sodium chlorid to the liter of water. This is, to start with, from two to six times the concentration of the ordinary, so-called physiological saline solutions, which, it will be recalled, contain from 7 to 9 grams of salt to the liter. When mixed with 8 or 10 liters or so of blood, however, the concentration is of course reduced. Fischer also rejects osmosis as an adequate explanation of cytolytic and similar phenomena, and opposes as unscientific, the common practice of restricting the intake of sodium chlorid in conditions of edema associated with nephritis. Many striking instances of success by following his methods have been reported; also many failures. No analysis yet made has given data whereby the conditions determining the success or failure can be exactly estimated. It is quite certain, however, that in many cases of acute nephritis, and especially in those resulting from the ingestion of such poisons as mercuric chlorid, a more or less continuous

administration of alkaline or alkaline saline solutions of moderate concentration is of considerable value. In chronic conditions, results are more variable, even in the individual case. Thus, in a case of chronic diffuse nephritis with uremia and general anasarca at Jefferson Hospital, the use of Fischer's solution by the rectum in moderate quantities, was accompanied with restoration of the urinary flow, disappearance of the edema, and return of consciousness. When continued, however, beyond this point, the rectum became intolerant, and the attempts being made to introduce some 250 mils. (0.25 liter) of the solution by hypodermoclysis, a subcutaneous tumefaction formed, which persisted for several days, and was dissipated only when distilled water (about 100 mils.) was injected into it. Absorption was then rapid and complete

This illustrates, in part, what I mean by the unknown factors.

In the limited time assigned to my portion of this discussion, I can allude, and then only briefly, to but one more of the many interesting phenomena described in the paper of the evening—that of ionization. Practitioners are a little slow in applying this.

In an interesting series of studies of the effects of various ions upon the living cell made some eight or ten years ago, Wolfang Pauli investigated their comparative precipitating powers upon proteins. Dealing first with salts having the same kation (basic component) but different anions (acid component) he found that the precipitating power of such salts decreased in a certain order, according to the anion, and irrespective of the kation. Then, dealing with salts of a given anion and different kations, he found that the precipitating power increased in a certain order, according to the kation and irrespective of the anion. Hence he concludes that kations are the precipitants, the anions under these conditions being inhibiting agents; and he arranges them, as the result of many experiments, in definite series, the precipitating power of the kation increasing in the following order: Mg—NH_4—K—Na—Li; and the inhibiting power of the anions increasing as follows: fluoride—sulphate — phosphate — citrate — tartrate—acetate—chlorid — nitrate — bromid—iodid—sulphocyanid.

Thus, for example, the weakest precipitant (magnesium) could overcome the inhibiting power of sulphate but could not overcome that of acetate or any anion beyond, while even bromid, which inhibits all other precipitants, could not overcome lithium.

And from these and other experiments he deduces the laws that: (1) the effect of a salt upon a protein is made up in the main of the algebraic sum of the effects of the individual ions; (2) that anions and kations antagonize each other.

The fact that the sulphocyanid ion is of even greater inhibiting power than the iodid ion led Pauli to test its effect upon normal and pathological

animals. The sulphocyanid ion, when combined with an elemental kation, is non-poisonous, just as the ferrocyanid ion to which Dr. Leffmann has referred, and for the same reason that the cyanogen is firmly attached. In brief, Pauli found that sodium sulphocyanid tended to reduce blood-pressure and to prevent deposition of calcium in the arterial walls, so that it could be used with good clinical results in cases of arteriosclerosis. He found also that sulphocyanids were even more active than iodids in favoring the formation of readily soluble protein compounds with the heavy metals, and thus favoring elimination in cases of chronic poisoning. Other considerations besides those referred to enter into this problem, as into that of decalcification, and time for their detailed statement is lacking, but the whole subject comes under the head of ion-colloid reactions, which are so important alike to the pathologist and the therapeutist.

Before leaving the subject of the sulphocyanid ions, however, a warning should be given. Whereas sodium sulphocyanid may safely be administered in doses up to 1 gram daily, for sedative and analgesic, as well as pressure-lowering effect, yet any compound of the sulphocyanid ion with an ester will produce almost instant death, owing to the solubility of the cell-lipoids in esters. Dr. Leffmann referred to the theory of narcosis by lipoid solvent substances and this is a further illustration.

It may be concluded, then, that while therapeutic application of the experiments of the physical chemist must be made with caution and reserve, and while we must always bear in mind the great difference that exists between living and non-living matter, and especially our ignorance concerning the many factors that complicate the physicochemical problems of the living body as contrasted with the comparative simplicity of laboratory conditions, yet nevertheless these experiments point the way to therapeutic as well as pathological progress. We should welcome every item of additional information, and we are under obligations to Dr. Leffmann for the clear exposition he has given us tonight.

I would ask him further, since so many of the physicochemical problems of living cells turn upon the question of alkaline or acid reaction, if he will not, in closing the discussion, elucidate that subject for us, from the modern viewpoint. If I am not mistaken, this is quite other than that which many Fellows of the College were taught in their student days. For instance, they were told that a solution of caustic potash (now called potassium hydroxid) was alkaline because of its potassium, that element being a typical alkali; while sulphuric or phosphoric acid owed its acidity to its high oxygen content. Now it is taught that the degree of acidity of any solution depends not upon the misnamed oxygen at all, but upon the relative concentration of active hydrogen ions, and alkalinity upon the concentration of active hydroxyl ions in which the hydrogen is

anchored to oxygen. Hence the solution of potassium hydroxid (KHO) is alkaline, not because of its potassium (K), but because of its hydroxyl (HO), and the high acidity of sulphuric acid depends not upon its sulphuric oxide at all, but upon the great quantity of hydrogen ions dissociated in the solution. Water is typically neutral, and in a certain sense it consists of H plus HO; but whether it can be said that the two ions here counteract one another, or whether the composition of water is to be viewed from a different angle entirely, I cannot pretend to say. I only want to emphasize the fact that in applying such studies as those of Dr. Fischer, it is important to bear in mind the modern definitions of acidity, alkalinity, and neutrality. So in Pauli's experiments it seems strange to read that nitrate and acetate, for example, are ions inhibitive of precipitation, when we daily use nitric acid and acetic acid to precipitate albumin out of urine. But in acetic and nitric acids, we have according to the modern view, hydrogen acetate and hydrogen nitrate. Hydrogen is the kation, and if arranged in Pauli's series, should be placed as the strongest of all precipitants when ionized. Thus, too, we find acetic acid a more delicate test for albumin than nitric acid, because the acetate ion has less inhibiting power than the nitrate ion. So at least, it seems to me. I should like to have Dr. Leffmann's view.

Dr. Alfred Stengel: The subject of physical chemistry, as Dr. Leffmann has said, is a very new science and one which to the best informed is a difficult and abstruse one, and one which those of us not technically interested in chemistry and physics can hardly hope to master, even in its more elementary particulars. But there is great reason for practical physicians to know something about the principles of physical chemistry and the newer principles of physics. One topic to which no particular reference was made by the author has been suggested by the remarks of Dr. Cohen—the use of saline solutions. This is one of the operations which we all, as physicians, are in the habit of resorting to—very often with the barest knowledge of the principles involved. The use of solutions of greater concentration than the solutions of the body either as enemata, subcutaneously, or still worse, intravenously, may be positively harmful. A solution to be absorbed from the intestine had better be hypotonic—below the concentration of the blood, or in the case of hypodermoclysis, isotonic. The introduction of hypertonic solutions subcutaneously, as in the experiment Dr. Cohen referred to, would usually result as in his case. There would be a precipitate—using a crude term—which subsequently might be dissolved by injecting distilled water. The introduction of hypertonic solutions into the blood stream, as advised by some French clinicians, while sometimes carried out apparently without damage, is a questionable procedure.

A second topic, interesting from the standpoint of Dr. Leffmann, is the

question of mineral waters. Many of the so-called mineral waters are claimed to have a radium content. While this may be present in some instances, it occurs to my mind that oftener there may be something in the ionization that makes for the effect in different cases.

Another aspect of the question of physical chemistry was that brought out by the pharmacologists, particularly of the Vienna School, especially with regard to the hypnotic substances and their absorbability by the lipoids of the central nervous system.

An argument in favor of physicians knowing something about the newer sciences is found in the application, the principle of adsorption to the combat against certain bacteria. Some bacteriologists have used fuller's earth in the treatment of local infections and proved it of value in combating diphtheria and typhoid carriers. By the administration of fuller's earth the bacteria have been removed in a way that chemical antiseptics are incapable of doing. The reports of Hektoen and some others open up a large field for development. The thought occurs to my mind whether or not some of the insoluble substances, such as bismuth and chalk, which are used in diarrheal diseases, may not act in the intestinal tract in this way.

Finally, I would refer to the very wide field that has been opened up by Ehrlich in the matter of chemotherapy. This comes closely upon the topic of physical chemistry. Investigators the world over are busying themselves with substances, which in themselves harmless, are capable of entering into physicochemical combinations with tissues either of the body or bacteria or other invading microbes and so rendering the invaders innocuous. The whole subject of physical chemistry is surely one which has a direct practical interest to physicians. It is a subject so attractive that one is perhaps a little prone to theorize and form hypothesis with little foundation.

Dr. Thomas McCrae: It certainly behooves a clinician to tread very warily when discussing the points which have been brought before us tonight. We have probably all been impressed by the way in which the essayist has brought abstruse problems before us in very simple terms. One danger to which many of us are exposed, not only in respect to the application of physical chemistry but in other problems, is of picking up terms without learning their meaning. This subject of physical chemistry lends itself to that. It is easy to talk about ions and ionization without having a clear idea of what is meant; of colloids and crystalloids without having any clear conception of their meaning. In the paper everything discussed is made absolutely clear. Ionization has a tremendous bearing upon the bodily activities. Without that, a great deal of the every-day work of our bodies would cease. Perhaps we are all familiar with the fact that ionization and electrolysis are closely connected. "Electrolysis puts life into the proteins."

The problems are many. The whole question of the relationship of the ions to edema, diuresis and glycosuria may be considered in this connection. Dr. Stengel referred to the use of hypertonic solutions. An interesting work is that done by Rogers in the giving of hypertonic solutions in the treatment of Asiatic cholera, in which his results justify the treatment. Another point emphasized by Dr. Stengel is the danger of introducing substances under the skin, one example being calcium lactate. I think the danger of such a method cannot be too strongly emphasized.

The whole subject of osmosis, important in animal life, is perhaps more important in plant life. Dr. Leffmann referred to the amount of lipoids in the cell wall. In the plant cell we have cellulose. The problem of diet is also closely concerned with this subject. We have a great deal in practical medicine to learn from physical chemistry. In speaking of colloids and crystalloids we must have some conception of what we are dealing with, must consider how much of the activity of our cells is due to difference in pressure. In clinical medicine we should do our best to make use of this knowledge because it would lead us in many instances to a much more rational therapeusis.

Dr. Joseph Sailer: This is a profound subject. I say this, not in the way of excuse, but as a result of what I have heard tonight. The subject illustrates first of all that the medical profession must take toll of all sciences for the better understanding of disease and the welfare of the human race. I agree heartily with Dr. McCrae, that we are prone to use terms with which we are not fundamentally familiar. We apply them to our therapeutics and believe we are using physical chemistry when we are really working with something concerning which we know very little. And then among many physical chemists there is a great difference of view. Results of experiments upon non-living matter must not be too freely applied to the living tissue. We must remember that the physical chemistry of living tissue is not yet a very clear factor. It is interesting to hear a paper such as this of Dr. Leffmann's. It throws light upon subjects that have been obscure. We must not imagine that a superficial knowledge of this subject will clear up every problem and that we can thereby get away from empiricism and back to science; which, however, is the aim of every one of us. I am reminded of an article written by Professor Cole on the structure of the atom. The fundamental thing in physics, in chemistry, possibly in the universe in some respects, is the atom, and it would seem that until we had a clear idea of the atom we could not go ahead in the solution of these problems. The article was illuminating to me in showing very clearly that our knowledge of the constituents of the atom is at present exceedingly inadequate. I am not a physical chemist or a physicist, and yet the terms involved in the subject are not all beyond my comprehension.

At the present time the atom is regarded as an exceedingly complex affair. It is said to consist of a central body around which are a number of minute bodies. The central body is the positive; the minute bodies are the negative electrons. Another view is that the atom consists of a series of hollow spheres which are the positive electrons in the centre of which are the minute negative electrons. Another is that the atom is a highly complex organism; still another that it is composed of a nucleus which represents again the positive electrons. This nucleus is exceedingly small—$\frac{1}{10000000}$ mm. in diameter. The electrons revolve about the nucleus. If one flies off we have a positive; if one is added, a negative electrification of the atom. All this has impressed me with the difficulty of obtaining a very definite concrete conception of some of the problems of physics. Until we get this we are not at liberty recklessly to apply these methods with the idea that we are making use of some tremendous scientific advance in medicine. Nevertheless, the application of the definite facts of physical chemistry is an exceedingly important thing. Practically, x-rays and all forms of radio-activity are nothing else. Although radio-activity is used therapeutically, more or less empirically, as a branch of therapeutics, it has proved useful. In the same way these other facts will have to be decided by empiricism before we can determine their value.

Dr. Leffmann (closing): I have only to say that the discussion has taken the direction that I hoped it would—the further development of instances of the application of physical chemistry. Care has been given to the interpretation of phenomena by physicochemical methods and criticisms have been made of the want of definiteness in certain directions. Each one knows how extensive the amplifications of the sciences are and how impossible it is for us to keep up with more than one narrow specialty.

SOME PHYSICAL FACTS ABOUT THE RADIO-ACTIVE ELEMENTS AS APPLIED IN MEDICINE[1]

By WILLIAM S. NEWCOMET, M.D.

It is the desire in this paper to bring before this body a few of the more common misconceptions that seem to exist regarding these radio-active elements.

There is a general impression throughout the medical profession that radium and the allied elements are bound up in a mystery, that the natural laws governing them are past their comprehension, and that they must be used in a mythical way to obtain results. Let it be understood that the sooner this mystery is set aside, the better it will be for the medical profession; and, perhaps, those who are exploiting radium by their assurance that they possess the only obtainable supply, will be the sufferers.

It is, however, most unfortunate that the supply of radium is so scattered, and some institution could accomplish a bold stroke for mankind if it could centralize or develop an institution where radium and its allied elements could be obtained and employed strictly for what they are worth, divorced entirely from all tendency of exploitation. The expense of maintaining a proper plant would be enormous in proportion to the amount of work accomplished, but so long as radium remains in the hands of private institutions, or worse still, in private hands, just so long will its usefulness be impaired.

The use of these elements medically must be divided into two divisions: (1) for the purpose of radiation; and (2) for employment as medicine internally, depending upon either the

[1] Read November 3, 1915.

radiation or perhaps, as with other drugs, to some extent the base itself.

First let us consider its local use, where it controls or is supposed to control certain pathological processes by the radiation of certain rays, the principal one being the most penetrating of all rays, the γ-ray, analogous to Roentgen rays. A second ray known as the β-ray is a ray analogous to the cathode ray, but here again it has a greater power of penetration, and it no doubt plays an active part where these radio-active elements are employed. A third ray, the α-ray, is practically worthless in external applications, although 90 per cent. of the energy of these radio-active elements is of this form.

Where these elements are to be used for their radiation the usual form of application is a small flat disk for surface radiation, or small tubes where deeper radiation is desired. The applications are to a certain extent merely a makeshift and are adopted according to the part to be radiated. While fulfilling a purpose, they do not meet the issue to the same extent as in cases in which the separate radium elements are employed and the application molded according to the necessities of the individual case; for instance, if it is desired to insert a given amount of radium into a tumor the strength of 200 or 300 mgs. may be placed in a glass tube which can be slipped into the eye of an ordinary surgical needle of fair size; and, furthermore, if it is lost, it need not cause alarm. Again, if it is desired to cover a flat surface, a certain dosage, a given size, all that is required is to charge a small piece of metal with the "active deposit" which is left in place for a certain length of time, and the patient can keep this piece of metal as a souvenir of the occasion. Not until we have such methods established in our midst will it be possible to obtain results that justify confidence.

No doubt, many of you have conceived the idea that it is the desire to give radium or these radio-active elements as souvenirs. Not at all.

It must be remembered that radium is merely the parent, that it merely gives forth the elements that give rise to the "active

deposit" and while all the therapeutic activity depends upon them, their life is short, and therefore they soon become worthless. In the meantime these elements have again recovered and are ready for further manipulation.

The thorium elements, unfortunately, undergo disintegration in a rather irregular fashion, and therefore do not permit the manipulation which is so convenient in this radium group; and, while the rays of thorium are still more penetrating than those of radium, its use must be confined to the applicator method, and furthermore, its manipulation from a chemical standpoint is difficult.

While it is not the province of a physician to carry out the difficult proceedings in the preparation of these different products, we should have established in our midst, laboratories where these preparations could be obtained and measurements made as the occasion demanded.

The following instance illustrates, for the sake of protection, the need of such institutions. A few months ago a dealer in this city had two tubes of radium for sale. The reason given seemed sufficient. He stated that they had originally been purchased from a well-known chemical house, the price being $400 and $1400. Tests were made and it was found that the amount was frightfully small compared with the price asked. He was therefore advised to send them to Washington for collaboration, for if he sold them legal possibilities might develop. A few weeks later the tubes were promptly returned to their owner, and the dealer who had always been careful of his reputation, was profuse with his thanks for the advice. The value of the radium in the tubes was 40 cents and $30, respectively. Is it any wonder that a plea is made that those using these radio-active products should familiarize themselves to some extent with the physics or leave it alone? Imagine a patient being treated with 40 cents worth of radium. Is this not sufficient reason that a central station should be established to prevent such exploits? Many of you are familiar with several such occurrences in the past, but that these tactics still prevail is past comprehension.

While the external use of radium seems to have many pitfalls, the internal employment has many more. Of this, the following is an example. About a year ago a certain physician in this building stated that he possessed a tube of radium which in the daytime he used for the treatment locally and which at night he placed in a jar of water. He then gave this water to his patients and from it he claimed to have obtained some brilliant results. Furthermore, he stated that he had measured the activity of the water. There seems to be a confusion between the so-called rays that emanate from the different radium elements and the emanation which is an element and a gas—subject to all the laws of all other gases, and consequently when confined within a tube cannot escape. Therefore the water did not contain emanation. The question in therapeutics still remains: From what did these patients derive their wonderful results?

We little realize what valuable waters Philadelphia possesses. Any number of persons seem to possess radio-active water by the barrel.

In the internal administration of radium or thorium certain facts must be taken into consideration, inasmuch as it is the radio-activity and not the elementary base that affects the system, for the quantity is too inconceivably small to be considered from that point of view. Therefore it would appear that the alpha radiation of these elements might be responsible for any physiological or therapeutic activity. This being so, in what forms then is it possible to bring it into the system; then, in turn, how does it leave the system? Like all agents of this class, this is by far the most important question.

Here again we come to a point needing the most careful study: For example, radium may be given as a salt, which may be either soluble or insoluble; or, it may enter the system as a gas in the form of the emanation. These salts give off the emanation in proportion to their age, and continue to give in a definite ratio indefinitely, or as long as they are contained within the system. It must be remembered, however, that insoluble salts allow only about 2 per cent. of the emanation to escape, the rest being

occluded within the walls of the powder unable to escape. If a salt of radium is administered naturally its elmination is by the natural channels, while the emanation formed by it during the time it is in the system is mostly eliminated by the lungs. On the other hand, if the emanation is given during that cycle of time it remains within the body the "active deposit" is thrown down, it being a solid is eliminated as other solids.

Therefore upon comparing the two methods of administration we have—radium, emanation, and "active deposit;" while with the second we have emanation and active product. Radium may be obtained in solution, the strength is easily calculated, and the dosage estimated accordingly. Its strength, after it has obtained its equilibrium, is more or less constant. It does not degenerate, at least, for a few hundred years. Being in solution it is absorbed and carried by the blood stream throughout the body. Just what effect the sulphates of the body have upon it is not definitely known. Some claim that it is eliminated promptly; others that it extends over days and weeks and so on. While in the body it is giving forth its activity, changing slowly into the emanation, the emanation in turn to the "active deposit." Now, should an insoluble salt be administered it passes along the alimentary canal unabsorbed, but it gives off the emanation and active product which are absorbed. It still holds, however, that the major portion of this emanation remains occluded within the intermolecular spaces of this insoluble powder. Its effects continue until it is eliminated.

But how about the emanation? Here the question is quite different. Although given in solution, water containing emanation, must be used at the source with as little agitation as possible; for, like all gases, its solution depends upon all the other natural laws plus those of the rapid disintegration. When it cannot be obtained directly from a spring the ordinary commercial emanator should be used under the best conditions. It is not a very efficient piece of apparatus, and some of the types placed upon the market are ridiculous. To have a very efficient activator would require one with some skill in its manipulation. Unfortunately, the

efficiency depends again upon employing the soluble salts. In the soluble radium salts under the best management about 20 per cent. of the emanation will be lost. When you consider that the insoluble salts are usually employed, and that only a 2 per cent. efficiency can be obtained at best plus the 20 per cent. decrease, it would seem that very little is obtained for the outlay. But the point is that when the emanation is to be employed this offers the only practical means of obtaining it.

The emanation taken into the stomach is rapidly absorbed, passes through the system, and in a very short space of time is eliminated by the lungs. Needless to state that its action is transient, and that repeated doses are needed. Sipping moderate quantities of water charged with the gas seems to be the adopted method.

It has been used in baths and inhalations. These methods perhaps might prove useful in the hands of very careful operators, but for general use their efficiency is doubtful. Here attention might be called to the existing conditions in the use of the thorium salts, for if these elements ever become of therapeutic value, these facts will prove most useful. The average life of radium emanation is about five and one-half days, while that of thorium emanation is seventy-six seconds. Now suppose we should take a certain amount of radium emanation into our system. During the time which it remains a certain amount of "active product" is formed, but the chances are that most of it will be eliminated as emanation. On the other hand, if thorium emanation is taken into the system, the greater portion passes over into "active deposit," while little of it escapes, the cycle of time being too short. Needless to state that the same principle is employed in the thorium emanator, they, however, are in turn less efficient than those for the radium emanations.

The desirable product for the internal administration of thorium is thorium X. It has about the same period of life as radium emanation. Therefore, when it is employed the patient must be close to the source of supply. Since it is a salt instead of a gas, it remains within the system undergoing a very rapid change

to emanation and "active deposit," and for this reason the thorium product is more powerful than the analogous radium product.

In these elements we have extremely powerful agents which cause profound systemic disturbance. Their value as therapeutic agents has by no means been established. Yet they are being employed throughout the country for the relief of these distressed individuals by persons who have little comprehension of the consequences. There is not the least doubt that they are of value, but like all other materials used in our medical arts, the results are in proportion to the skill employed in their use.

The object of this paper is to draw attention to a few facts frequently confused; and while it is realized that there are many more points to be covered, the few to which allusion has been made emphasized the magnitude of the subject. Fortunately, where these articles have been used, the dosage no doubt has been small, and the baneful effects, if any, have been inconsequential. Likewise, the good that might have been expected failed for the same reason.

DISCUSSION

Dr. Solomon Solis Cohen: The College is very much indebted to Dr. Newcomet for his clear and cogent demonstration of a subject concerning which there is much looseness of expression and much confusion of thought.

My own experience having been confined, within recent years at least, to the use of radium emanation water, I shall not attempt to say anything concerning external irradiation.

In estimating the value of any method of treatment which is to a certain extent new or unfamiliar there are certain difficulties: One arises from the extravagant statements of those who use it without much thought of what is to be expected and without much ability to criticize results. Another, equally unfounded, however, arises from the skepticism of those who have made no use of the method but deny its value *a priori*. But, the greatest difficulty of all, I think, arises from its use, even by intelligent persons, with extravagant expectations of what is to be accomplished. Failing to realize such expectations the method is condemned as valueless.

No physician is likely to mistake an automobile for an aëroplane; and all recognize that to condemn an automobile because it cannot fly is illogical. But I do believe that many physicians condemn the use of radium, because it doesn't fly when it shouldn't be expected to fly.

Radium emanation water acts largely—at least I think it does, although we cannot be certain—by the diffusion of the alpha rays or particles, and the ionization of the blood and of the salts of the blood which takes place in consequence. Just how that produces its therapeutic effect I do not know and I have not seen any convincing explanation. I have seen guesses and speculations, and I am quite able to indulge in guesses and speculations, myself, but I have seen no convincing study. All we know certainly is that we introduce the substance into the system and that in some pathological conditions, certain definite changes may reasonably be expected to follow—although not in every case. In my early experience with radium emanation water, in a few cases of arteriosclerosis and in a few cases of high tension from other causes, in which it was used, a marked lowering of blood-pressure was observed. In other cases exactly similar in every respect, so far as I could tell, this effect was not produced, and I am as yet unable to say why it should have occurred in one case and not in another. It may have been a matter of dosage, or there may be other factors which, as yet, are not apparent.

One thing, however, is true: The early use of radium emanation water and of so-called "radio-active" bottled waters, was attended with considerable disappointment from neglect of those facts to which Dr. Newcomet has drawn our attention, especially the short life of the emanation. In bottled waters—if present at all—it had probably disintegrated to the inert point before the water came into the possession of the dealer, and in water taken from various forms of apparatus, the manner of preparing it, of drawing it off and of administering it was such that the virtue was largely, if not entirely, dissipated before reaching the patient. Also, even when all the precautions were observed in its preparation, and its transmission and its administration the actual therapeutic efficacy of the small quantity of radium emanation used was virtually *nil*. I have come to the conclusion that a dose of much less than 10,000 to 20,000 machè units a day (equivalent to about 4 to 8 microairies) is of little benefit in the majority of cases.

Some of the apparatus upon the market probably hold no emanation at all. There are three forms of trustworthy apparatus that I have used. I have had the water from these tested repeatedly and we find that it does contain when freshly drawn the amount of emanation stated by the respective manufacturers. One of these instruments made in Pittsburgh was kindly loaned to me for use at Jefferson Hospital. Two others—

one made in New York City and one imported—were loaned for use at the Philadelphia General Hospital and some of all forms have been placed in the houses of patients who have purchased them or are paying rental for them. In selected cases of a limited number of affections, chiefly of the joints, and of certain metabolic aberrations, we do at the present time get reasonably good results in an uncertain proportion of cases—and that is all we can expect. If we ask infallibility of radium emanation, if we ask that every patient, no matter what is the trouble with him, shall get well, we shall be disappointed. In one case of long-standing osteo-arthritis of the spinal column and in a number of cases of arthritis deformans of the extremities I have seen excellent palliative results; better palliative results than I know how to obtain by other means. Also in a number of gouty patients, there has been considerable amelioration. I have seen no case of gout cured by radium emanation water. I have seen no case of arthritis deformans or of any other chronic affection of the joints or chronic metabolic disturbance cured by means of radium emanation water. But I have seen sufficient palliation in cases otherwise resistant to treatment to make me believe that we have in this agent, when properly used, in a conservative way, with not too extravagant expectations a useful addition to our armamentarium. When applied with due obedience to the physical laws governing its action, with due regard to its chemical and mechanical properties, and in sufficient quantity, we can get results in these conditions that are worth while, and that makes me think it also worth while to extend our investigations, and to determine whether or not the agent has power in other directions. But we must remember that it is of limited power and that it must be used with discretion and with intelligent appreciation of the laws underlying its action.

Dr. A. B. Hirsh: I wish to ask Dr. Newcomet his opinion of the *intravenous* injection of radium as recommended by some commercial concerns which send out so-called literature quite extensively. A recent issue of the *Journal of the American Medical Association* contained a caution on this mode of administration because of our lack of knowledge of the end action in the economy of radium where administered in this form.

Dr. Newcomet (closing): I did not attempt to speak upon the physics of radium. This subject was presented to us a year or two ago by Dr. Goodspeed, and at that time the different methods of measurements were given. I desired to call attention, as Dr. Cohen has emphasized, to a number of mistakes made in the use of radium preparations, and especially to emphasize the desirability of establishing a central station for supply, so that every physician might obtain radium, thorium, or

other agent in desired amounts, and possessing therapeutic activity. Regarding the question of the intravenous injection of these salts, I mentioned that we have the soluble and insoluble salts of radium and the gas, the emanation. It must be remembered that radium sulphate is the most insoluble salt known. Just what effect the sulphur and sulphur acids in our economy have upon radium combined with these products of disintegration, such as the emanation, "active deposit," is still unknown. Certainly they must be given with judgment. I think this answers Dr. Hirsh's question.

CREEPING ERUPTION (LARVA MIGRANS) OF THE SKIN, PARTICULARLY IN REGARD TO ITS HISTOLOGICAL FEATURES

INCLUDING THE DEMONSTRATION OF THE BURROWS AND THE LARVA IN THE EPIDERMIS[1]

By FRANK CROZER KNOWLES, M.D.

The subject of larval infection of the skin is one not only of interest to the dermatologist but also to the entomologist and the pathologist and should prove instructive to those interested generally in medicine. The various dipterous invasions which lead to a destructive or purulent inflammation, resembling furuncles, abscesses and doughy tumors, such as are caused by the Africa Cayer worm, the larva of Ochromyoma Antropophaga (Blanchard), the various muscidæ, the hypoderma bovis, ver macaque, etc., are so diverse in their clinical aspects from the present case that they will not be considered in the present communication.

Creeping eruption which is a special variety of animal parasitic infection is of rare occurrence. The causative larva has been discovered by but five investigators, namely, Sokolow, Samson, Wosstrikow and Bogrow, and Rudell; the first four being Russian and the fifth an American. The histological examination has been successful in but 3 cases including the present instance. Complete microscopic findings, including the demonstration of the burrows, have been performed by Lenglet and Delaunay,

[1] Read November 3, 1915.

Rille and Riecke, and the writer. The efforts of Dickinson, T. Fox and Duckworth who examined the tissue from Lee's first case were negative, and Hamburger was able to demonstrate, in his example of the affection, only the phenomenon of an acute inflammation of the skin. The writer, alone, has been able to discover the larva in sections.

The first case of this disease was reported by Robert Lee in 1874, under the caption "Creeping Eruption;" Crocker recorded an instance in 1892, terming the disease "larva migrans;" Sokolow recorded cases in Russia in 1888; Neumann reported an instance in 1895; Kaposi reported the first case in Austria in 1898. The first American cases were reported by Van Harlingen in 1902; Stelwagon in 1903; and Hamburger in 1904. Other American cases have been recorded by Shelmire, Hutchins, Moorhead, Gosman, Haase, Rudell, and Kirby-Smith. The disease has also been reported from Bulgaria, France, the Congo, and Arabia. The disease is rather prevalent in eastern Russia, Samson saw 9 cases in three years, 1 of which was from the western portion of Russia and 1 from Bulgaria. Sokolow has seen 2 or 3 yearly. Wosstrikow and Bogrow have met with 2 or 3 cases in Russia, each year during the last two decades.

The disease is particularly prone to attack children, although in Russia, young peasants working in the fields furnish most of the cases. According to Hamburger, of 11 cases in other countries than Russia, up to 1904, 8 occurred in children.

The seat of predilection for the attack is the uncovered portions of the body, particularly the hands, the feet, and the face, although quite a number of instances have been recorded on the buttocks or near the genitalia; 5 out of 11 cases developed in the latter region (Hamburger). According to Rille and Riecke, the axillæ and pubic region may be attacked. No burrows have ever been reported on the scalp or bearded region. Samson has recorded cases in which the mucous membranes of the mouth, nose and conjunctiva have been attacked.

Creeping eruption may be initiated with an itching sensation, but more often the case comes to observation a considerable period

after the burrowing has been inaugurated. Frequently a red creeping line reveals itself without subjective symptoms. More often, however, a finger-nail-sized red spot appears from which the line takes its beginning. Lee demonstrated a small slightly reddened papule and of the size of a shoe-eyelet. According to Van Harlingen it starts as a vesicle.

The beginning line is light red while the older portions of the channel are of a dark-red shade. The line is from 1 to 4 mm. in width and 0.25 to 0.5 mm. in elevation. According to Hamburger the line is surmounted by a vesicular formation. Van Harlingen also found vesicles caping his line which suggested somewhat the burrows of scabies. Stelwagon and also Lee found a bead-like appearance, suggesting in the latter case the appearance of a lymph channel. Bruno discovered little irregularities along the track of the line which he considered as points of defecation, thus heightening the resemblance to the lesions of scabies. In most of the cases the burrows are unbroken.

The characteristic symptom is the progressive character of the burrow. Sokolow believes that the beginning burrowings are always in a straight line and toward their end they become wavy. In the majority of cases only one red line is observable. In the cases of Crocker, Rille, Stelwagon, Haase, and Rudell two lines were present, while in those of Kaposi, Schmidt, and the writer three lines were demonstrated.

The development of the line takes place with varying rapidity, now curving and looping, now adopting a straight course and traversing in twenty-four hours from 1 to 17 cm. The greatest progression having been observed in Crocker's and Lee's cases, seven and four and one-half inches respectively. The line does not branch. It may remain passive for hours and even days and then resume its gyrations. The progression of the line may only be observed during the night, as in Haase's case, or greater progress may be made during this period, as observed by Rudell. As the red line proceeds the older portions fade, leaving a pigmented tract behind. As a rule the burrows are very superficial and the erythema is generally removable on pressure. Notable exceptions were,

however, observed by Sokolow who recorded a case in a brunette which showed distinct scarring. Schmidt also recorded a resulting cicatrix.

In regard to the length of progression of the larva, in Crocker's case the burrowing was followed over a period of two and one-quarter years; after covering a large portion of the cutaneous surface it only ceased its activity by an accidental suppuration in the neighborhood. The reverse was observed in Matchinsky's case, in which the activity of the larva was limited in its gyrations to the cheek, for a period of two months.

According to the Russian authorities the larva resides from 0.5 to 1 cm. from the end of the burrow. Samson states that by putting pressure on the skin and employing a magnifying glass, the larva can be seen in some cases as a black point in the unaffected skin slightly in advance of the actively growing end of the channel. This black point was observed immediately in advance of one of the burrows in the present case.

Two cases of this affection have been under the care of the writer, both occurring in children, the second of which forms the basis of this communication.

G. D., a well-formed girl, aged twenty months, visited my office September 6, 1912, with a typical case of creeping eruption, which had started August 22. The serpigenous, gyrating lines, there were three distinct burrows, involved palm-sized areas on both buttocks, and the upper portion of the mons veneris. The mucous membrane was unattacked. An attempt was made to destroy the *larvæ* with nitric acid, and as both applications proved a failure, Dr. Edward B. Hodge excised all three tracts. Four days after excision, insufficient tissue having been removed in front of the advancing end of one of the burrows, the larva made a fresh progression at the edge of the excision on the left buttock and burrowed down toward the lower edge of the left mons veneris, travelling a distance of two inches in twenty-four hours. Since the last operation there has been no recurrence.

The writer has had a very unusual opportunity for the study of the histopathological features of creeping eruption, as all the

passages were excised in their entirety. All of the tissue was cut serially and 3000 sections have been examined during many hours of the last three years. Quite a number of stains have been employed in order to bring out to the greatest advantage the various salient features. The investigation has been crowned with success, in that fully 150 sections show excellent views of the burrows and 30 present various portions of the larvæ. The excellent treatises of Rille and Riecke, and of Lenglet and Delaunay upon this disease, particularly that of the former, have been consulted freely and frequently and their findings coincide almost absolutely with mine, excepting that, in addition, I have been successful in finding the larvæ in sections. Their deductions form a partial basis for my results.

All varieties of passageways were found, longitudinal, transverse, and because of the winding character of the burrows and the various planes in which they were cut, those of a very irregular shape. Some of the channels were clear of contents, resembling markedly those found in scabies (Hartzell), others were partially filled, while the majority were entirely blocked up. The burrows were, however, quite different from those made by the acarus scabei in that they were much larger and were located in the lower portion of the horny layer at the junction with the rete and also in the upper portion of the rete Malpighii, rather than as scabies in the middle and upper portion of the stratum corneum.

As a general rule the upper boundary of the lumen consisted of a few flattened dark granular cells together with the horny layer. The floor consisted of rows of rete cells; in no place was the burrow in contact with the corium. The microscopic picture shows the passages in almost all sections to be located in the upper portion of the rete. The undermining work of the parasite was also found in a few sections in the lower portion of the horny layer exclusively. The diameter of the burrow varied from 0.25 to 0.75 mm.

The stratum corneum is not changed from the normal in breadth and thickness, excepting that it is bulged over the passageways. It was intact in all sections. The covering of the passage con-

sisted of elongated granular cells without a sharp contour but very distinct nuclei. These nuclei are flattened and some are almost linear. The lateral and outer bounds were chiefly com-

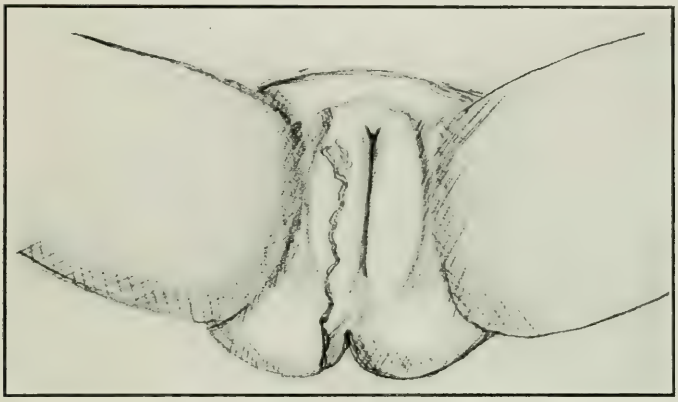

FIG. 1.—Creeping eruption involving right labium majus.

FIG. 2.—Creeping eruption involving the right buttock, showing the gyrating character of the track. The two dark spots are areas where nitric acid was unsuccessfully employed.

posed of separate cells of the stratum germinativum; epithelial cells, with distinct nuclei which are also mostly flattened. Both the upper and lower boundaries of some of the passages consisted

of cells of the granular layer. Three or four rows below the burrows the cells have a normal configuration. The remaining cells of the stratum germinativum and the basal layer are somewhat

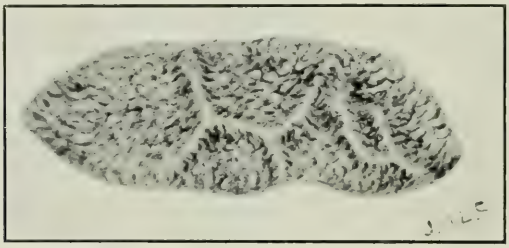

FIG. 3.—Drawing of excised skin, showing the appearance of the burrows through a magnifying glass.

FIG. 4.—Drawing through the microscope, showing a newly made burrow. The oval body, with the club-like projection, in the central and lower portion of burrow. Elongation and broadening of the rete pegs and a round-cell infiltration in the papillæ and upper corium, chiefly in the neighborhood of the bloodvessels.

edematous and the nuclei are found in a large degree to be undergoing mitosis.

The character of the contents of the passageways varies considerably; the new channels may be entirely free and open but as they become older they become more and more completely blocked. There is observed in comparatively newly bored channels a refract-

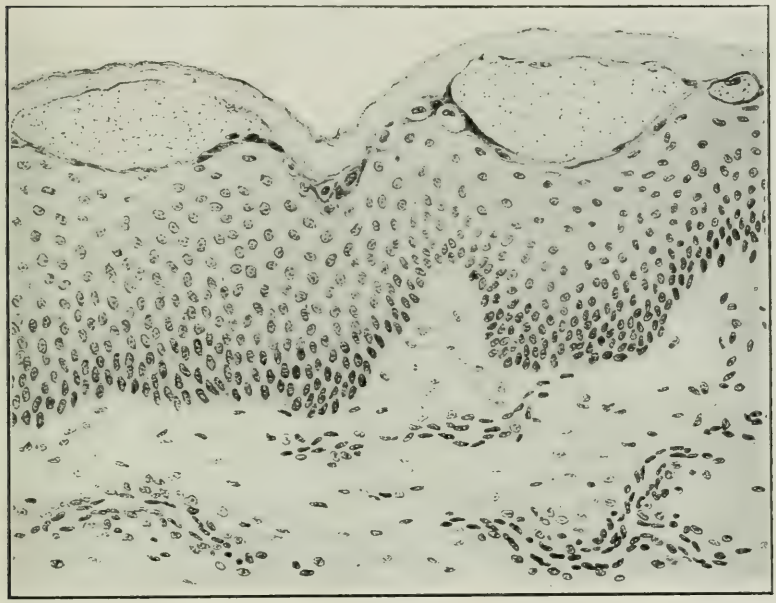

Fig. 5.—Photograph of histological drawing from the case of Rille and Riecke, showing a transverse section of three burrows, two large and one small, at the junction of the horny and rete layers. (Mraček's Handbuch der Hautkrankheiten.)

ing uniform substance which is broken up with numerous small round granules. Later these granules are observed to be of unequal size and shape, round, irregularly long, and oval. They are found in large numbers without a vestige of regular arrangement or grouping. Rille and Riecke suggest that they are of cell derivation probably a degeneration of the granules of the cell nuclei. It has occurred to me, as a possibility, that some at least are the

fecal discharge from the larva, as is found in sections in scabies. The passageways also contain swollen, degenerated, indistinctly outlined epithelial cells; numerous nuclei without a cellular surrounding, which vary considerably in their staining characteristics, some distinct, others only faintly colored; eosinophiles; and less numerously lymphocytes and polymorphonuclear leuko-

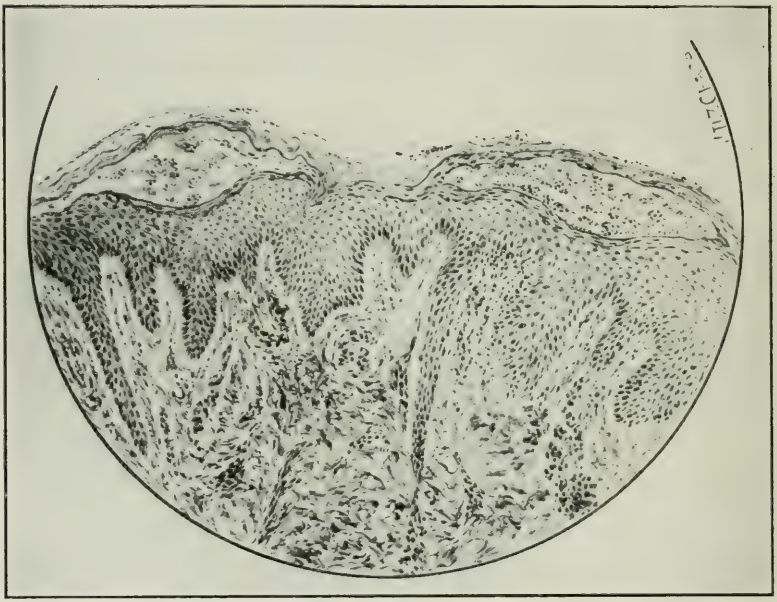

Fig. 6.—Histological drawing of writer's case, showing transverse section of two burrows, at the junction of the horny and rete layers. Older burrows than the other depicted, cavity completely filled. Widening of some of the rete pegs, elongation and narrowing of others. Round cell infiltration in upper corium. Compare with photograph of the case of Rille and Riecke.

cytes. The Mallory connective-tissue stain also shows a considerable amount of fibrin contents. There is a large amount of granular and cellular debris.

In the neighborhood of the burrows the rete pegs are either contracted and elongated or broadened, and there is therefore a corresponding contraction and narrowing of the papillæ. These changes are, however, found in only a portion of the sections.

There is a considerable diversity of pathological findings in the various fields, in some the corium is absolutely normal while in others there is an inflammatory accumulation of cells in the papillary layer. In some sections there is an accumulation of cells in the immediate neighborhood of the capillaries of the papillæ. These cellular infiltrations have also been observed

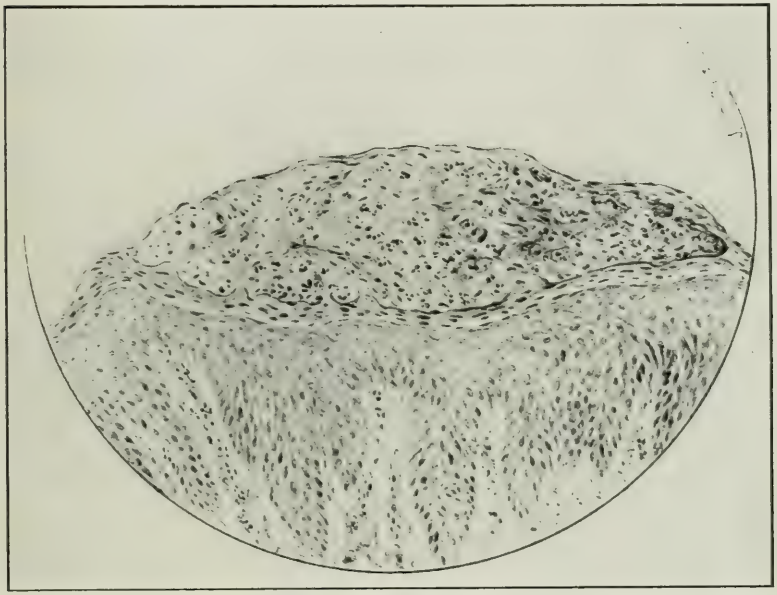

FIG. 7.—Drawing, under high power, showing a transverse section of burrow filled with irregularly shaped granules, swollen, degenerated, indistinctly outlined epithelial cells, numerous free nuclei, eosinophiles, lymphocytes, polymorphonuclear cells, fibrin, and granular and cell debris. Elongation of the rete pegs and a cellular infiltration in the corium is also seen.

surrounding the other bloodvessels of the cutis, peripherally around the hair follicles and the sebaceous glands. A few round cells were observed, in some sections, around the coils of the sweat glands. In a few instances the broadened pegs were invaded by a dense cellular infiltration which also extended considerably down in the corium. The greatest round-cell accumulations are found in the neighborhood of the papillary bodies, and then in

only a few sections, and only to a much lesser degree in other portions of the corium. The bloodvessels are dilated, with a surrounding cellular infiltration, some filled with blood corpuscles and others empty.

As the parasite which burrows in creeping eruption has never been discovered in sections, the writer has had to base his study

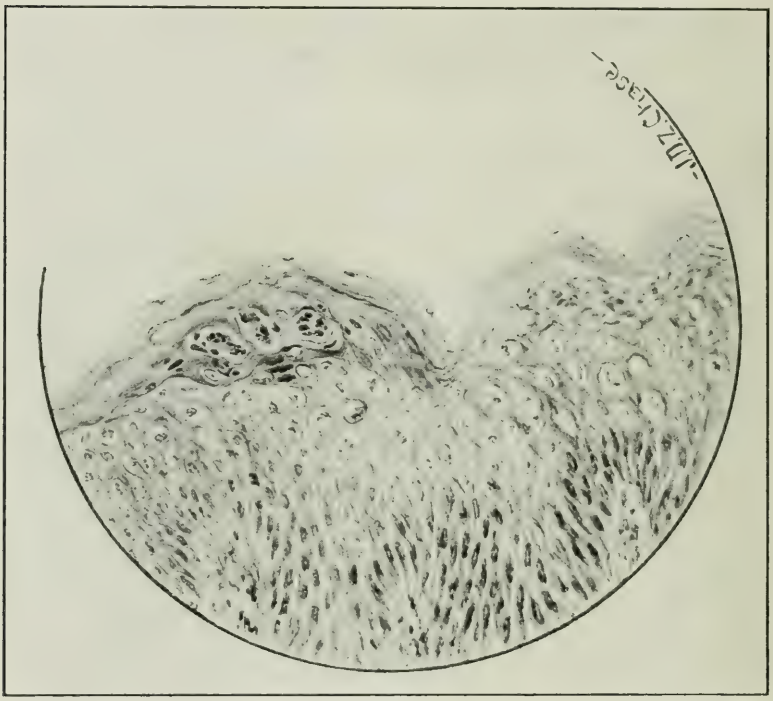

FIG. 8.—Drawing showing the three oval bodies, close together, in the rete, probably sections of the larva, referred to in the text. The numerous mitoses in the rete cells are also plainly shown.

upon the characteristics of the larva picked from the burrow and examined microscopically and for a working basis has had to study the acarus scabei, although quite different from the present larva, as it appears in skin tissue.

In about thirty sections, cut serially from the different passages,

there was found in the upper portion of the rete, with a few flattened epithelial cells above and the normal rete cells below, an oval body of a definite structure consisting of a granular-looking material and several dark points around the circumference and

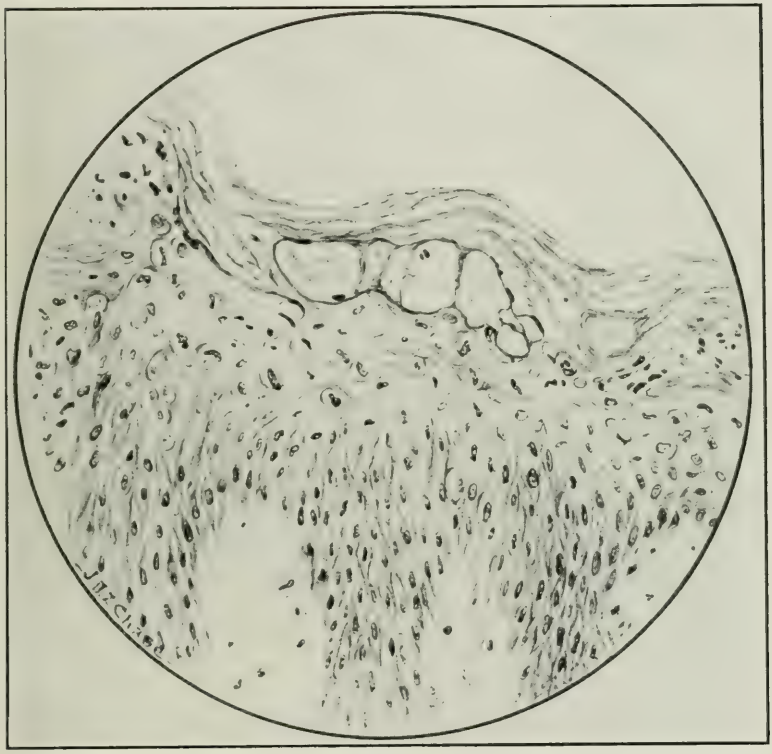

FIG. 9.—Drawing showing a longitudinal section of the larva; six sections of the body and the two club-like projections, which are characteristic of the tail of the organism are distinctly shown, located in the upper rete layer of epidermis. The rete pegs are elongated and numerous mitotic figures are seen.

an attached club-like projection closely conforming to the tail processes of the larva. This oval body with a distinct capsule was found in eight serial sections and is thought to be either an egg of the larva or a portion of the larva itself. In another series of sections, from another track, there were twelve serially cut which

showed three of these oval bodies, closely in contact, with the same characteristics of the one just described and in the same position in the rete. In still a third series of sections, from the remaining burrow, ten showed six complete segments of varying size, oval and somewhat irregular in shape, of the same texture of those just described, with two distinct club-like processes, the latter evidently the tail attachments of the larva. The latter was found in the upper portion of the rete in the same relative position as those that have just been mentioned.

The acarus scabei (Unna) has been carefully studied in section, and the organized body formation closely conforms to the first oval body depicted, although it has not the club-like projection. The latter series of oval and irregularly shaped bodies with the typical club-like tail projections conform so closely to the description of the larva migrans that I have no hesitancy in stating that all of these oval-like bodies are sections of this parasite, some, because of the gyrating channel and the various planes of the sections, showing a transverse, others a transverse and partially longitudinal, and still others an almost complete longitudinal view of the organism. Some of these oval-shaped and irregular bodies lay directly in the burrow, others were in immediate contact with it, while others were in the same location in the epidermis as the burrow was found.

The organism causing this affection was originally found by Sokolow and this author states that it measures 1 to 1.5 mm. in length and 0.5 mm. in width, it has ten segments, is provided with hooklets, better developed at the head end, which apparently possesses two suckers. At the tail end are two club-like processes. In the interior are two tubes.

The zoölogical classification of the parasite causing creeping eruption is still not definitely settled, although the majority of dermatologists and entomologists, particularly Cholodkowsky and Porchinsky, regard either the gastrophilus hemorrhoidalis or the gastrophilus pecorum as causative, notwithstanding the suggestion of Brauer and Handlirsch that it is of the genera Tetranychus and the species Telarius. As Sokolow found black nits on the hairs it points strongly toward the gastrophilus hemorrhoidalis.

Samson, and also Hamburger, give an explanation of the manner in which, probably, the patient is infected by the larva of the gastrophilus. The gastrophilus hemorrhoidalis, a species of estrus, deposits its eggs on the lips and the nose of the horse and the larvæ attach themselves to the bowel as well as the anus. The bot fly lays its eggs in the latter part of the summer and the larvæ are probably transmitted to the stomach of the horse where they attach themselves in varying numbers to the mucous membranes, and there they remain during the winter season. The next summer they loosen their hold, pass through the intestine, and burrowing into the ground, they further undergo metamorphosis into the pupa from which the imago or adult bot fly emerges in a few weeks.

A considerable number of the cases of this affection appear during the summer months, thus carrying out this theory that they are derived from the ground after passing through the intestine of the horse. Crocker and also Lenglet and Delaunay thought the snails resident in a vineyard were the hosts of the parasite. Stelwagon states that five patients of his, attacked by this affection, had been residents of a watering resort. As the majority of all of the cases have been reported in Russia in those laboring in the fields, this again tends to support the theory of origin as promulgated by Samson.

The incubation period of the disease is unknown. Crocker believed it to be from four to six weeks. Samson thought the shortest period of incubation to be six days. In the instance reported by Brodier and Fourquet it seemed to have been less than twenty-four hours, while Lenglet and Delaunay set a period of three days.

There is still a considerable amount to be learned in regard to this interesting affection. Creeping eruption is gradually, however, being elucidated, first with the finding and probably proper classification of the organism, then with the finding of the burrow in sections, and the present investigation showing the larva in epidermic tissue.

In closing the writer wishes to express his sincere thanks to Dr. Paul Lewis for the privilege of carrying out this study in the Ayer Laboratory of the Pennsylvania Hospital.

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THE OCCURRENCE OF MILIARY TUBERCULOSIS OF THE LIVER IN THE COURSE OF PULMONARY TUBERCULOSIS[1]

By ROBERT G. TORREY, M.D.

I HAVE recently made a study of a series of autopsy reports, giving the records of the findings in 131 cases of pulmonary tuberculosis. The object of the investigation was primarily to observe certain points of interest regarding the tuberculous involvement of the liver and other abdominal organs. Chronic tuberculosis of the liver with large masses of tuberculous material occurs commonly in certain animals, and a few cases have been reported in human beings; but this condition is so rare in man that it is considered as a pathological curiosity, and need not be considered in this discussion.

There is no dearth of literature regarding the frequency of occurrence of tuberculosis in the liver. Ullom's[2] article covers the subject with thoroughness, and Rolleston[3] gives an up-to-date *resume* of the subject, with references. White[4] has discussed thoroughly the occurrence of miliary tubercles in the liver in the cases studied by him.

It is generally recognized that the liver is involved by miliary tuberculosis in a large percentage of fatal cases, Rolleston putting the figures at about 50 per cent. and White as high as 80 per cent. The opinion of most authors leads us to believe that an involve-

[1] Read November 3, 1915.
[2] Amer. Jour. Med. Sci., 1909, cxxxvii, 694.
[3] Diseases of the Liver, Gall-bladder, and Bile Ducts, London, 1912, 2d ed.
[4] Fifth Annual Report of the Henry Phipps Institute, Philadelphia, 1909.

ment of the liver by a tuberculous process is a matter of little importance, and that for some reason it is likely to occur just before death. This view, which seems to be expressed by most writers on the subject, is far from satisfying. I am not aware that I have ever seen an explanation as to why a wide-spread miliary tuberculosis should occur just before death in the liver, though it does not develop in other organs which ordinarily do not show tuberculous formation, as the pancreas. Tubercle bacilli have been demonstrated in the bile, and they must be passed through the liver, more or less constantly, or deposited in its spaces throughout the course of chronic pulmonary disease.

Much work has been done on the question of the effect of tubercle bacillus in the production of fibrosis of the liver, and it seems probable, as held by Stoerck and others,[1] and as confirmed by the observance of Lavenson and Karsner,[2] that a gradual infection of the liver can take place with a disappearance of the tubercles as formed, resulting in a periportal fibrosis. This does not, however, in any way explain the facts found at autopsy, where we find, as a rule, a wide distribution of young miliary tubercles of approximately the same age, seeming to indicate an overwhelming infection. It would seem necessary to consider whether this condition can exist without serious result.

The following points have been observed: In the liver, miliary tuberculosis is usually demonstrable microscopically, the tubercles fairly young in state of development and occurring in the perilobular spaces, about the portal vessels, with the greatest frequency. The tubercles are usually not demonstrable grossly, unless there is present a miliary tuberculous peritonitis with invasion of the liver capsule. There may be perilobular fibrosis, and there is likely to be considerable degree of fatty change. In the kidney, tubercles are seen grossly in a much larger proportion of cases than they are found in histological examination, as noted by White. Occasionally old lesions may be seen on the kidney, either caseous or fibrous, or perhaps a single young tubercle, but in histological sections

[1] Wien. klin. Wchnschr., 1907, xx, 847.
[2] Univ. Penna. Med. Bull., Philadelphia, 1909, xxii, 167.

cut for the purpose of examining the kidney structure a tubercle has very seldom been encountered. In the spleen they are found much more frequently than in the kidney, and in the spleen they are older, as a rule, than in the liver. It is impossible to say just how old these gray tubercles found in the liver are, but in working with rabbits, Evans, Bowman, and Winternitz,[1] in studying the pathogenesis of the tubercle of the giant cell in experimental tuberculosis, find a beginning of tubercle formation within six hours after injection of the bacilli into the mesenteric vein and well-developed tubercles within forty-eight hours.

The 131 cases studied in this series have been divided into four classes:

Class A.—Cases apparently dying of pulmonary tuberculosis, showing miliary tubercles of the liver; these are, as nearly as can be determined from the autopsy records, and in some cases from a study of clinical histories, cases which may properly be said to have died from pulmonary involvement, that is, not dying from such intercurrent causes, as violent hemorrhage, advanced amyloid disease, severe pneumonia with acute consolidation of the lung tissue, etc. These cases all show miliary tuberculosis microscopically, but in comparatively few it is demonstrable grossly.

Class C.—These are cases which would be diagnosed at autopsy as more or less generalized miliary tuberculosis, usually showing miliary tubercles of the peritoneum, and possibly of the meninges, spleen, liver, and perhaps of the bladder; but here particularly are found cases of omental and peritoneal involvement, in which it seems that a spread to the liver by way of the lymphatics of the capsule has taken place. A marked point of difference between this class and the first is that in these cases the miliary tuberculosis present in the liver is nearly always recognized grossly. These cases all show miliary tuberculosis of the liver.

Class D.—These are cases of advanced tuberculosis where death is due to some intercurrent event, as acute cardiac dilatation, acute pneumonia, etc. (In this is included tuberculous pneumonia,

[1] Jour. Exper. Med., 1914, xix, 283.

where consolidation of both lungs is almost complete.) These cases do not show miliary tubercles of the liver.

Class X.—These are cases apparently dying from pulmonary tuberculosis in which tubercles were not reported on histological examination. It is difficult to classify these cases, but we feel that on the average it has been done fairly. There are probably several cases under "C" which really belong in classification "A," and there are some cases under "X" which should probably be placed in "D." Mention should be made of the question of tuberculous pneumonia, in which there was consolidation of nearly all of the lung tissue. This was considered as the cause of death under classification "D," but considerable degrees of consolidation, if of a tuberculous nature, have been classified under "A" or "X."

A summary of the results shows: "A," 49 cases; "D," 29 cases; "C," 33 cases; and "X," 20 cases. Eighty-two cases, or about 63 per cent., therefore showed miliary tuberculosis of the liver. What appears more significant, however, is that the 29 cases classed under "D," all of which showed active pulmonary tuberculosis, but with death from independent causes, or as the result of acute complications, none showed miliary tubercles in the liver. This is the point, suggested by this compilation, which demands explanation. It would seem that the liver can take care of a gradual tuberculous infection, but that a sudden and overpowering infection of the portal circulation overwhelms the liver resistance, and there ensues a sudden development of disseminated miliary tuberculosis. It is reasonable to assume that this must have a profound constitutional effect, and in the case of an individual weakened by a long course of chronic disease, this might readily lead to a fatal result.

Infection of the portal circulation may take place either from the intestines, which are nearly always infected, or from the spleen. Mechanically the ideal source of a massive infection of the portal stream lies in the spleen, in which the tubercles are apt to be comparatively large, of varying age, and lying in close relation to large blood spaces leading directly into the portal stream.

While it is unsafe to draw parallels between human tuberculosis and experimental tuberculosis in animals, the work of Lewis and

Margot,[1] showing an apparent increase in resistance to tuberculosis after the removal of the spleen in mice, suggests that the spleen may be a source of infection to the liver.

There is need for considerable research work to determine the part played by the liver in fatal tuberculosis. If this series of cases is representative, and if, as a rule, these findings are present, viz., that in cases dying from pulmonary tuberculosis there is usually present a wide-spread miliary tuberculosis of apparently recent onset, and in cases dying from other causes this is not found, we must consider two possible explanations for these findings: (1) that in cases dying from tuberculosis, the liver tissue, for some reason, loses its resistance to the tubercle bacilli shortly before death, and at the same time is freely infected through the portal circulation, or (2) that in these cases the liver is able to cope with a gradual infection, but a sudden and overwhelming flooding of the portal stream with the tubercle bacilli overpowers the hepatic resistance, allowing tubercles to develop, and that the reaction in the liver has a severe constitutional effect, often determining the fatal issue.

In view of the fact that we do not find miliary tuberculosis developing in the liver in cases of active tuberculosis dying from independent causes, and that other tissues of the body are not rendered susceptible to tubercle development with the liver as death approaches, the latter explanation seems more reasonable than the former. I think it probable that such infection takes place by way of the portal circulation, and probably very frequently from the spleen. This view accords, in a measure, with the observation that experimentally the development of fatal tuberculosis is delayed by the removal of the spleen.

I desire to express my sincere appreciation to Prof. Allen J. Smith, at the University of Pennsylvania, both for valuable suggestions and for placing at my disposal the autopsy records of the Pathological Department of the University, and to Dr. H. R. M. Landis, director of the Phipps Institute of the University of Pennsylvania, for allowing me to refer to the autopsy records of that institute.

[1] Jour. Exper. Med., 1915, xxi, 84.

Cases apparently dying of pulmonary tuberculosis and showing miliary tuberculosis of the liver on microscopic examination:

CLASS A

1900—	26	
	34	
	54	
	35	Tuberculous pneumonia.
1901—	64	
	86	
	91	
	107	
1902		
(?) —	5	Pneumonia and disseminated tuberculosis.
	73	
1903		
(?) —	12	Locomotor ataxia.
1904—	15	
	24	
	26	
	35	
	37	
	66	Miliary tuberculosis of lungs and pneumonia.
	79	
	98	Tuberculous pneumonia.
	120	
	132	
	157	
	158	
	202	Tuberculous pneumonia.
1905—	1	Acute parenchymatous nephritis.
	6	Tuberculous pneumonia; endocarditis (mitral).
	27	Hemiplegia; amyloid; tuberculous pneumonia.
	90	
	108	
	112	
	123	
	138	
	157	
	4659	
	4587	
	4522	
	4500	
	4462	
	4460	
	4380	
	4306	
	4281	
	4282	
	4272	
	4248	Recent hemorrhage, eight ounces.
	4232	Chronic advanced pulmonary tuberculosis. At right base there is pneumonic consolidation, but no microscopic examination of ungs (pneumonia?).
	4198	Also amyloid liver and spleen.
	4155	
	4148	Hypernephroma of kidney, but thoroughly encapsulated and no metastasis.

49 cases

Cases of more or less generalized tuberculosis, usually showing involvement of peritoneum and omentum, or of general miliary tuberculosis. All show miliary tuberculosis of the liver:

CLASS C

1900—	61		1904—	142
1901—	28			170
	114			174
	124			190
	214			196
	220			213
1902—	6		1905—	3
	75			9
	191	Peritonitis.		46
	212			47
	245			49
1903—	152			69
1904—	9			110
	17			126
	63			140
	110			—
	117			33 cases
	131			

Cases of pulmonary tuberculosis dying from other causes and not showing miliary tuberculosis of the liver on microscopic examination:

CLASS D

1900—	55	Advanced amyloid, aortic, and mitral valvulitis (veg.), hydropericardium; tuberculosis (primary); epididymitis, and scrotum.
1901—	48	Ulcer of stomach and hemorrhage into pancreas; chronic and
	154	acute miliary pulmonary tuberculosis, and abscess; perforation of esophagus.
1902—	15	Rheumatoid arthritis; advanced amylosis of liver, kidney, spleen, etc.
	16	Diabetes; pulmonary gangrene.
	30	Chronic pulmonary tuberculosis; acute bronchopneumonia; acute infiltrated liver; portal space infiltrated.
(?)	65	Cancer of bowels; edema of lungs (?); tuberculous ulcer; mesenteric nodes.
	182	Pyelonephritic tuberculosis; subacute fibroid pleurisy; edema of brain (?); tuberculosis (?).
	202	Psoas abscess; miliary tuberculosis of lungs; chronic mitral valvulitis; pulmonary hemorrhage.
1903—	42	Pulmonary tuberculosis; pneumonia.
	154	Acute dilatation of heart following operation of glands of neck.
1904—	6	Nephritis; dropsy; operation for decapsulation; pulmonary fibrosis and fibroid tubercles.
	18	Operation on tuberculous shoulder-joint followed by miliary lungs and bronchopneumonia.
	86	Tuberculous meningitis; internal hydrocephalus.
	105	Tuberculous pneumonia; complete of right and almost complete consolidation of left.

1904—	147	Cardiac hypertrophy; valvulitis; bronchopneumonia; tuberculosis.
	171	Hypertrophy and dilatation of heart; hydropericardium; tuberculous pneumonia.
	184	Fibroid tuberculosis of left lung; miliary tuberculosis of right lung; edema and congestion; mitral and aortic disease; nephritis.
	187	Myocarditis; acute endocarditis; chronic bronchitis; both apices.
(X) ?	216	Fibroid and fatty heart; calcified aortic leaflets.
	233	Septicemia; peritonitis.
1905—	15	Amyloid spleen, liver, kidney; carcinoma of uterus and kidney.
(X)	26	Tuberculous pneumonia; tuberculous spleen; pyothorax. (One liter of pus.)
	44	Tuberculous vertebræ; amyloid liver, kidney, and spleen—advanced.
	64	Pulmonary tuberculosis; tuberculous pneumonia; pulmonary congestion; brown atrophy of heart; chronic nephritis. Aged eighty years; tuberculous spleen.
	106	Miliary tuberculosis of lungs and peritoneum; acute nephritis; death following operation on ileum and sigmoid; no tubercles in spleen.
	159	Empyema; collapse of lung; cloudy swelling of kidney; tuberculous kidney and spleen.
	4364	Tuberculous pneumonia, acute; both lungs practically solid.
	4243	Acute pneumonia; sudden death.

29 cases

Cases in which death seems to be a result of pulmonary tuberculosis and which do not show miliary tuberculosis of the liver on microscopic examination:

CLASS X

1901—	5	Apparently pulmonary tuberculosis, but also edema of brain and gelatinous pneumonia. (Microscopic.)
	36	Fatty and parenchymatous degeneration of liver.
	103	
	117	
1904—	42	Tuberculous meningitis. (Miliary tubercles.)
	100	Acute parenchymatous nephritis.
	116	Cardiac fibrosis; bronchopneumonia.
	130	Myocarditis, fibrosis, and fatty infiltration.
	176	Brown atrophy of heart; fibroid lung (left); ulcerative tuberculosis of right lung.
1905—	13	Chronic myocarditis; chronic diffuse nephritis.
	33	Tuberculous pneumonia.
	36	Nephritis; myocarditis; pulmonary edema and congestion.
	135	Tuberculous pneumonia of right lung (1120 grams), entirely solid; left, slight.
	4415	Pathological diagnosis written by pathologist personally states miliary tuberculosis of liver; detailed report does not state.
	4345	Amyloid liver, spleen, kidney, intestines, etc.
	4287	Few tubercles, grossly. Not reported microscopically.
	4224	Typical course of chronic pulmonary tuberculosis; tuberculosis in liver reported grossly, but not mentioned in histological report.
	4197	Same as 4224. Reported grossly.
	4221	
	4316	

20 cases

DISCUSSION

Dr. Allen J. Smith: I appreciate Dr. Torrey's presentation of this subject of the curious fact of the frequent appearance of tubercles in the livers of individuals dying apparently from the exhaustion of a long-continued pulmonary tuberculosis, while in individuals with pulmonary tuberculous involvement but in whom some intermittent affection or accident closes the case, the liver is found without such involvement. As far as the mode of infection of the liver is concerned I am disposed to accept Dr. Torrey's belief that this is due to hemic transference. Believing in the frequent dissemination of tubercle bacilli by the blood I would accept the possibility of dissemination from the lung to the liver by arterial route, and, would also recognize the transference by route of the portal venous blood from the intestines and from the spleen. While the extension from the intestine by the path suggested is probable, I call attention to the possibility of the reverse, that is, the infection of the intestine by tubercle bacilli which gain access to it from the liver by the bile ducts. I refer to personal observation of tubercle bacilli in the bile of the gall-bladder in human beings without grossly visible tubercles in the hepatic substance and of tubercle bacilli within the lumen of intrahepatic gall ducts in sections of the livers of experimentally inoculated guinea-pigs. Doubtless intestinal tuberculosis is usually the result of swallowing tubercle bacilli; but biliary concretions should also be recognized as a possibility.

If the belief in a tuberculous bacteremia be correct, one must believe from the data of autopsies, as these dwelt upon by Dr. Torrey, that the liver is naturally a structure with relatively high resistance to tuberculous infection. Following this line of thought we may suppose that for a time the bacilli brought by one of the blood structures to the liver are either destroyed by the organ or discharged with the bile; that later, if here and there infection actually takes place, the tubercles are early destroyed and the reaction here may be the source of the cirrhosis which is not infrequently met in the livers of pulmonary tuberculous cases; and that finally, when through repeated insults of this type or through the effects of the mixed toxic factors of the disease the resistance of the organ is much weakened, the rich transmission of bacilli from the spleen or ulcerated intestine, as Dr. Torrey suggests, may induce at the close of life the persistent crop of tubercles to which his paper calls attention.

One will readily believe, too, that in the course of such processes other changes are induced in the hepatic tissue, perhaps without demonstrable structural changes, perhaps with alterations (as, for example, the fre-

quently seen steatosis of the liver of pulmonary tuberculosis), which may decidedly lower the metabolic ability of the organ, and it is easy to imagine that the emaciation and exhaustion of an advanced case of pulmonary tuberculosis is due to such hepatic complication more than to the pulmonary changes themselves.

Dr. William M. L. Coplin: I recall two cases of tuberculosis of the liver manifesting unusual features. One, a girl, aged fourteen years, at operation showed extensive miliary tuberculosis of the peritoneum with voluminous ascites. The serosa was studded with gray tubercles. Nodules were present which when examined macroscopically led us to believe that they were composed of tubercles within the liver. A fragment was excised and intrahepatic tubercles and contained bacilli were demonstrated. That patient is alive and well, having recovered from the tuberculous peritonitis as well as from the lesion in the liver. She has since married and borne children. Specimens from the other case I have shown to some of the gentlemen present. The liver contained tubercles clearly of different ages; some were old, partly fibroid, and surrounded by fibrous capsules. There was also present a much more recent group which had developed apparently shortly before death. It was clear that the organ contained at least two crops; possible a number of disseminations had occurred.

There is another point concerning which I should like to ask Dr. Torrey, namely, with regard to submiliary deposits in the liver. I have not found the so-called submiliary tubercle of the French writers so frequently as it is said to occur.

Of special interest in this connection is the widely discussed relation of lipoids to immunity and especially to the immunity of tuberculosis. It may be that in certain extremely fatty livers frequently found in patients in whom all conditions appear favorable for the development of hepatic tuberculosis, the liver escapes because of the intracellular lipoids. I do not recall an instance of intense miliary tuberculosis in a very fatty liver. The livers that contain tubercles are usually not universally or notably fatty, and I suspect that some of the immunity to which Dr. Smith has referred may to some extent be due to, or influenced by, the rich lipoidal content of the organ.

THERAPEUTIC SIGNIFICANCE OF A CONCEPTION OF HODGKIN'S DISEASE AND ALLIED AFFECTIONS BASED UPON CLINICAL AND EXPERIMENTAL EVIDENCE[1]

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Clinical, pathological, and experimental studies made during the past seven years have led to a working hypothesis that will serve as a tentative definition of a group of closely related affections, of which Hodgkin's disease may be taken as the most characteristic example; a non-communicable infectious granulomatous process due to the B. hodgkini (or to similar or as yet undifferentiated microörganisms), protean in the resultant local (tissue) and general reactions and therefore in clinical manifestations. In this category, the reasons for which will develop later, have been placed leukemia, more certainly the lymphogenous, and barely possibly the myelogenous, pseudoleukemia, chloroma, mycosis fungoides, Banti's disease, some forms of lymphosarcoma, certain arthritides, and a type of recurrent elephantiasis-like cellulitis. So far as can be determined, none of these diseases has ever progressed to the point of certain diagnosis and has been known to undergo spontaneous resolution.

Observations made throughout the world at various times since the development of modern pathology have repeatedly suggested a common cause for most of these diseases and indicated their

[1] Read December 1, 1915. This work has been aided by a grant from the Rockefeller Institute. It is a pleasant duty to acknowledge great indebtedness to the Trustees and Superintendent of the Milwaukee County Hospital for providing opportunities for experimental work and the production of immune serum.

possible identity. Little will be presented, however radical it may first appear, that has not already been advanced by accepted authorities save the claim that the etiological factor has apparently been discovered and that a more satisfactory method of treatment is thereby made possible.

The following necessarily brief summary of the combined observations of a group of coördinated workers can only give the most significant points that are believed to have been established, without any attempts to present substantiating evidence in detail.

From a clinical view-point this infectious process is characterized by fairly constant features, not always equally well developed and usually to some extent obscured by chronicity. The progress of the disease is not steady but marked by alternating periods of aggression and remission. In the earlier stages and in the more chronic processes the periods of remission are longer—indeed, so long as to raise hopes of recovery in some instances, and the aggressive phases so slight and so brief as to be attributed to other causes if noted at all. Later in the course of the disease, or in the more acute forms, the aggressive phases become dominant and may mask the recessive periods so completely that they can escape even fairly careful observation. Three quite distinct stages are usually to be recognized, and to them Trousseau's classification based upon his original observations in 1870 are today equally applicable. The first or latent stage is marked by a gradually developing lassitude with periods of malaise, usually afebrile, and a slight anemia. The second or progressive stage may supervene gradually upon the first or occur suddenly, explosively, as Trousseau aptly described it. Now the dissemination or intensification of the process is unmistakable, the lassitude amounts to distinct disability, the periods of malaise are pronounced, frequently with a low fever, and there is evident anemia. A third or cachectic stage, unfortunately often too prolonged, is marked by emaciation, extreme anemia and great physical and physiological disability, and is almost constantly febrile. All forms have been universally fatal unless properly treated, and in Banti's disease alone has ultimate recovery been accepted.

Bunting's work as a basis of explanation of these phenomena is most important, and his observations have been so satisfactorily controlled that confirmation should follow when his methods are adopted.

The anemia is of a secondary type, but may approach the primary form in extreme cases, and is the result of a hemolytic action of the toxin. This toxin, in fact the organisms themselves, have an affinity for lymphoid tissue, wherein the lymphoblastic and endothelioid cells are particularly affected and fibroblastic proliferation commonly induced. Similarly the megalokaryocytes of the bone-marrow are irritated and the eosinophilic and neutrophilic leukoblasts directly or indirectly involved. Thus there develops a blood picture which is characteristic not only for the typical and some at least of the atypical forms of Hodgkin's disease, but also for its stages, and its final disappearance is, we believe, the only index of complete recovery. Sufficient data have not yet been accumulated to warrant more than a presumptive speculation as to the variations in tissue response to this toxic irritation. However, it may develp that at one extreme excessive lymphoblastic response may determine a lymphatic leukemia or pseudoleukemia, at the other extreme an endotheliomatous hyperplasia simulating a neoplasm may result from a selective action upon the endothelioid cells. In the middle ground would stand Hodgkin's disease proper, in which all the cells mentioned respond to the irritation. The nature and extent of this response determine, according to this conception, not only the acuteness of the process, and its stages, but also the clinical picture.

Pathologically, there is definite confirmation for the foregoing assumptions. In Hodgkin's disease there are four quite distinct types of lesion, stages in the development from the earliest to the latest or possibly from the most acute to the most chronic.

The first has been described clinically by Benda, Chiari, and Bunting, and has been reproduced experimentally in our work. The other three are well established. Atypical lesions are remarkably numerous, and since apparently they may devleop as the result of favorable therapy, it is fair to assume that they may be the

result in part of variations in virulence and resistance. These histological variations from the usual lesions may be so great as to render a positive microscopic diagnosis in our present state of ignorance uncertain or even impossible. An unmistakable if temporary metamorphosis of a typical Hodgkin's disease blood count to that of lymphatic leukemia in a patient whose necropsy established the correctness of a diagnosis of Hodgkin's disease is significant in this connection, and is also indicative of the close relationships of these processes. Sarcomatous degeneration has been described, notably by Karsner. Our observations in this particular have been limited, but such evidence as has accumulated, clinical, pathological, and experimental, is against this view unless our conception of the distinction between the dissemination of a granulomatous process and of a neoplasm is erroneous. Evidently if our observations are correct, Mallory's assumption that these diseases are tumors is untenable.

Since Bunting obtained the B. hodgkini in February, 1912, he has been able to cultivate it from all fresh affected tissue wherein the histological diagnosis was positive or when the blood picture of the patient was characteristic, unless that tissue has been contaminated or had been recently actively treated by the *x*-rays. In his absence, cultures made from a gland excised from a patient who had recently been given immune serum remained sterile.

He has recovered it in pure culture five times from one individual at various intervals extending over three and a half years, three times from another and twice from two others. Recently one of our earliest patients, from whom a mass of cervical glands had been removed eight years previously, suffered a relapse and the organism was obtained from an axillary enlargement. Other morbid tissues have been subjected to culture and dissimilar diphtheroid organisms have been recovered, but never when there was neither histological nor hematological evidence of their specific activity. An organism morphologically identical has been stained *in situ* in tissue showing the characteristic changes. This may be the only organism identified and in some acute cases may occur in profusion.

In the early attempts to reproduce the disease by inoculation of animals excessive amounts were given and resulted in the development of atypical but still characteristic lesions of the early or acute stages. Incidentally the peculiar affinity for lymphoid tissue was evidenced. More recently in conjunction with Dr. Kristjanson at the Milwaukee County Hospital the inoculation of dogs with small doses over many months has produced more chronic changes in the germinal centres in lymph glands and in the spleen which Bunting holds to be identical with those occurring in Hodgkin's disease and Banti's disease respectively. Moreover, these experimental animals and one normal man who was given a polyvalent vaccine prepared from similar organisms all developed the characteristic blood changes, the man reverting to normal after the vaccination was discontinued. None of these effects have been obtained by the use of other organisms, though observations in this particular are as yet incomplete.

Much has been stated about the great numbers and wide distribution of diphtheroid organisms, all of which is granted. The strains that we hold to be of etiological significance are possessed of a distinct cultural individuality, with their reluctant growth restricted to few media. They appear to have slight variations physically and culturally which have as yet been incompletely determined, but they have been tentatively grouped, and as these groups correspond to some extent with the lesions from which they were obtained, it is assumed that there is some variation in the toxins produced.

Olitzky observed that the organisms which he had obtained gave positive results in complement-fixation tests with the sera of immunized animals but not with the serum of patients suffering from the disease. Sera obtained from patients under our friends' care as well as our own were submitted to Dr. Kristjanson, who tested them with antigens prepared by Prof. McJunken, of Marquette University, and by Prof. Clark, of the University of Wisconsin. Apparently a positive reaction resulted only when a patient was at or just beyond the height of an aggressive phase of the disease. The sera from animals under inoculation all gave positive results.

The serum from a fairly highly immunized horse, with normal horse sera as controls, showed that a fairly specific agglutinin was resident in the immune serum. No bactericidal or bacteriolytic powers were demonstrable.

From what has been stated or implied there is some justification for the assumption that the B. hodgkini or closely related organisms provoke a series of reactions that have common clinical manifestations, positive and negative phases, three well-marked stages, peculiar tissue and blood changes and a fatal termination. Variations in the clinical picture are held to be attributable in part to differences in the toxins of the several strains of organisms thus far secured and in part to differences in the native resistance of infected individuals and the method of infection.

Owing to these considerable variations in the histological and hematological reactions and the differences in the strains of diphtheroids whose etiological relationship remains to be determined incontrovertibly, we believe no diagnosis is positive until at least two of these three diagnostic factors (hematological, histological, and bacteriological) are positively established. It must be remembered that tuberculous adenitis may imitate this disease so accuretely as to be indistinguishable clinically, that rarely a diphtheroid infection may be added to a tuberculous, though the reverse of this sequence is perhaps more common.

Treatment has been based upon the hypothesis that there is a portal of entry for the infection with subsequent dissemination by direct extension, and lymphogenous or hematogenous bacterial metastases. Protective reactions are seldom if ever adequate to overcome the disease. Therefore it is attempted when possible and feasible to locate and to remove the portal of entry, commonly the tonsils, to excise when indicated and as completely as possible all of the approachable affected tissue in order to place the balance of power rapidly and materially on the side of the individual, and then to follow with *x*-ray exposures, hygienic measures, and the intravenous administration of immune serum.

This after-treatment must be continued relentlessly for years if ultimate cure is to be obtained. The blood picture has been the

surest means of estimating the individual's condition and gives the earliest warning of an impending recrudescence which occasionally can be averted.

A study of our experiences and a review of the literature have indicated that certain more or less generally accepted therapeutic measures are harmful or futile. Arsenic is of benefit solely as a tonic. The administration of salvarsan is of no lasting if any benefit. *X*-ray treatments must be given as an adjunct measure, since no cure due to this agency alone is on record. Drs. Baer and Foerster, who have done this part of the work, will publish the methods they have applied so successfully. Aside from burns, the progress of the disease may be affected unfavorably by ill-advised roentgenological treatment. Partial excisions are as indefensible as in cancer therapy, and this applies equally to the removal of test glands. A probable diagnosis can be obtained from the clinical history, the blood picture, the reaction to tuberculin and physical examination. If radical treatment be indicated, a primary excision with frozen section diagnosis may immediately precede it. Otherwise there is nothing to be gained for the patient but a probably certain diagnosis at the risk of a grave dissemination of the process. The only justification for routine test gland excisions, the preparation of an autogenous vaccine, has been eliminated from our work.

Vaccine treatment, autogenous or polyvalent, subcutaneous or intravenous, intensive or extended in acute, chronic or convalescent cases has never produced *per se* any detectable improvement in individuals we have treated; indeed, if the blood picture is the criterion we now believe it to be, actual harm has been done in some instances. Although the administration of Coley's mixed toxins preceded improvement in one case of the lymphosarcoma type, its routine administration has not seemed to be indicated, though we still would use it in suitable cases.

A brief outline of our results will serve to give some evidence in support of this working hypothesis and to indicate that there is reason to hope that a cure for some of these hopeless diseases is not purely an optimistic fantasy. A cure is considered estab-

lished only when a patient has been without demonstrable evidence of the disease, including a normal blood picture, for five years.

GROUP I. *Type, Hodgkin's Disease.* Probably sixty or more cases have been seen. Some were in a dying condition, others refused treatment, in a few palliation was attempted with some temporary relief, occasionally a considerable prologation of life under less trying conditions. In ten cases radical treatment was attempted. One child, aged five years, succumbed to operation and three subsequently died of the disease. Four are living and in good condition from one to eight years since treatment began, one with excellent and the others with good prospects of ultimate recovery. Two very early cases are cured. Three of the ten cases have been given immune serum. In one the administration was discontinued on account of urticaria; in another both glands and spleen enlarged primarily, subsequently to recede almost to normal. A gland removed soon after the last dose of serum gave a pure culture of B. hodgkini. The third developed a multiple glandular enlargement during the injections which finally disappeared except in one cervical node. This was excised. Histologically it showed a very chronic type of lesion, and cultures from it remained sterile. Incidentally, there was in this instance an improvement in the blood picture.

GROUP II. *Type, Lymphosarcoma.* Three cases have come under our care. One was given a course of vaccine (autogenous), refused further treatment after a severe reaction from one dose of Coley's toxins, and has since died. One is greatly improved, particularly after two series of immune serum treatments. Benefit in this man followed a course of Coley's toxins at a time when a fatality seemed inevitable, but intensive *x*-ray treatments were also given and were probably to some extent the cause of improvement. The present prognosis is good. In the third case the process apparently was still confined to one tonsil, though a positive blood picture had developed. This individual is temporarily relieved, has a normal blood picture and should ultimately be cured.

GROUP III. *Type, Lymphatic Leukemia, Pseudoleukemia, Chloroma.* One case of chronic lymphatic leukemia in the late

stage of the disease is undergoing his second course of immune serum injections. Curiously he was having a recurrence of an atypical remittent form of fever simulating the variety which Murchison first described as characteristic of Hodgkin's disease, and which is improperly called Pel-Ebstein. In this case also the glandular enlargements increased after the first course of serum, subsequently to recede. One case of pseudoleukemia (identical with lymphatic leukemia save for an absence of lymphocytosis) was seen in terminal stages of the disease. A course of immune serum was without appreciable effect. Death occurred two weeks later. One case of chloroma was recognized. Treatment was refused; death ultimately occurred from nephritis. Marked permanent improvement followed three injections of an autogenous vaccine but is attributable rather to a recessive phase that persisted until death.

Group IV. *Type, Banti's Disease.* One case was seen at the Milwaukee County Hospital. Splenectomy was followed by recovery and a return to a normal blood picture. Cultures were positive as they were from two or three other spleens sent to Dr. Bunting, the third remaining sterile. This lesion, we believe has been reproduced experimentally in dogs by frequent intravenous inoculations extending over long periods. A progressive secondary anemia also developed.

Group V. *Type, Chronic Hypertrophic Arthritis.* We have seen one case in which a diagnosis was made accidentally. Inguinal glands were excised in an attempt to obtain a streptococcus for a vaccine, but from the glands B. hodgkini grew in pure culture. This tissue was positive histologically and a characteristic blood picture was found to be present. Marked subjective improvement followed a course of immune serum when subcutaneous and intravenous administration of an autogenous vaccine had failed some months previously to have any appreciable effect.

This type of joint lesion developed in one monkey that was being inoculated subcutaneously. In one other subacute case recurrent attacks of acute arthritis occurred during periods of aggression. Death occurred before any chronic changes had developed.

GROUP VI. *Type, Elephantias-like Cellulitis.* One case of an obscure nature that had been under observation for seven years was also diagnosed accidentally from tissue removed to obtain an autogenous vaccine. Typical organisms were present in pure culture and the blood picture was characteristic. Improvement in this patient was noted subsequent to intravenous autogenous vaccination. Infection is still present but in a comparatively avirulent form, and the prognosis is excellent.

GROUP VII. *Type, Mycosis Fungoides.* The one case seen with Dr. Foerster was in an advanced stage, though still free from skin ulceration. One course of immune serum seemed to relieve an intense pruritus to some extent and was followed by a marked reduction in the induration and pigmentation of the skin but without effect upon the numerous enlarged glands. Lesions in a skin nodule and in lymph glands were histologically positive, and from a lymph gland the organism was obtained in pure culture.

In all of the above cases the diagnosis has been established if our premises are correct, and from all but three the B. hodgkini was obtained. Two of three were treated before this organism had been discovered, and the third had no tissue excised from which to make cultures.

In conclusion, it may be stated that if it is impossible to reproduce these lesions by the inoculation of organisms other than the B. hodgkini, its etiological relationship will have been established. Granting that this may be the fact, the prospect for an efficacious curative serum is at least encouraging, but even if this be untrue, it has at least been demonstrated that Hodgkin's disease, contrary to the accepted belief does not result in an inevitable fatality in less than five years, but is curable when recognized early; and even when treated later, fairly normal health may be obtained for eight or more years.

DISCUSSION

Dr. Richard M. Pearce: I think the most interesting thing about this presentation is that we have listened to an account of Hodgkin's disease by a man who has continuously and without interruption devoted eight or nine years to the study of this disease. Such concentrated study by clinicians is not uncommon abroad, especially in Germany, but little of such work is done in this country. To hear the story, as we have tonight, from every point of view—bacteriological, pathological, clinical and surgical, with attempts at vaccine, serum and *x*-ray treatment—is most inspiring as an example of what a busy surgeon can do, if he has the desire, in connection with his daily clinical routine. From this point of view, and without regard to the question as to whether or not all the statements Dr. Yates has made will eventually be confirmed, I believe it one of the most interesting communications we have had here for some time. The investigation of those diseases which occur only in man and cannot readily be reproduced in animals must be developed by the clinician and surgeon, and Dr. Yates has shown us how such investigation may be prosecuted.

As to the evidence which Dr. Yates has presented, there is some doubt in my mind as to whether pathologists and bacteriologists will at once accept the views as to etiology. Diphtheroid organisms are ubiquitous and are so frequently found in the fluids and tissues of the body under so many conditions that many doubt their importance as specific etiological factors in disease. That vaccine treatment proved of little value is not surprising. On the other hand, the very special action of the serum which Dr. Yates describes is most important and his observations cannot be lightly dismissed. I am not sure that he has been wise to group so many allied conditions in the discussion of Hodgkin's disease. It befogs the main issue somewhat and weakens the argument in favor of specific etiology. Still, Dr. Yates's experience gives him a deeper insight in the problems of Hodgkin's disease than have most of us and I feel we can look forward to his further study of this disease with confidence and the hope that many of its problems are nearing solution.

PROCEEDINGS

OF THE

SECTION ON OPHTHALMOLOGY

DECEMBER, 1914, TO DECEMBER, 1915

DECEMBER 17

Homonymous Crescentic Scotomas in Association with Ethmoiditis and Tooth-root Abscess

Dr. G. E. de Schweinitz related the case history of a man whose ocular examination developed the fact that to the right side of each fixing-point there was a crescentic scotoma, larger in the left than in the right field. Ophthalmoscopic examination was negative. General examination yielded negative results except the detection of an ethmoiditis, and after proper *x*-ray examination abscess cavities at the apices of the roots of the incisors and cuspids on both sides. Proper treatment of these dental and sinus lesions was followed by very prompt subsidence of the visual difficulties. He thought that the bacterial elements of toxins which caused the lesions which were interpreted by the scotomas originated in the ethmoidal disease and oral sepsis. When this source of infection was removed by appropriate treatment, the formed lesions disappeared and the restoration of visual function took place. He discussed at some length various forms of hemiopic scotomas, among others those which occur in pituitary body disease, and suggested as an explanation of the peculiar shape of the scotomas in the visual fields of his patient,

that these crescentic defects represented parts of a ring-shaped scotoma, the left half of each ring either not having been developed, or the ring being complete, the left segments had disappeared before the time of examination. He referred to the fact that these so-called ring-shaped scotomas had been reported in connection with ethmoiditis and sphenoiditis on several occasions, and that he himself had placed upon record one case of this character.

Concerning Increased Intra-ocular Tension in Association with Exudative Choroiditis

Dr. G. E. de Schweinitz presented a series of case histories illustrating the rise of tension which frequently occurs with exudative choroiditis.

Dr. Holloway stated in reference to paracentesis in these cases, that several years ago a case came under his observation that began with an enormous choroidal exudate and ultimately developed all the manifestations of a serious uveitis. Owing to persistent high tension, paracentesis was done. With the first escape of aqueous the whole lower portion of the iris became intensely engorged and of a dusky red color. The engorgement also extended along the peripheral lateral portions of the iris. The manifestations were so threatening that only a very small amount of aqueous was permitted to escape. The same phenomenon occurred on two subsequent occasions when paracentesis was attempted.

Dr. Holloway also referred to what might be described as a paradoxic action of mydriatics and myotics in certain cases of uveitis. He then referred to a case of uveitis he had observed some eight or ten years ago and which Dr. de Schweinitz had seen in consultation with him. In this case there developed an increase of tension, and eserine invariably produced a further rise in tension. After first trying the effect of homatropin, scopolamin was used and in each instance the tension was promptly reduced.

Dr. Posey said that he had under his care at present a case, which presented many points of similarity with some of those

just mentioned, of a man in middle life, with so-called serous iritis, in whom eye tension was high throughout the course of the disease, finally yielding, however, to the repeated and continued use of myotics. He had attributed the rise in tension to a blocking of the anterior filtration zones by inflammatory matter. Although it was possible and indeed likely that the choroid was involved, such involvement was so far forward that it was invisible to ophthalmoscopic examination.

Exophthalmos of High Degree Caused by Large Mucocele of Frontal and Ethmoidal Cells

Dr. William Campbell Posey gave the notes and presented photographs of a woman, aged sixty-nine years, upon whom he had recently successfully operated for an enormous mucocele of the left frontal and ethmoid cells. The swelling occasioned by the mucocele was so great that the globe was displaced at least two inches in a downward and forward direction, and its movements so restricted that some downward and inward motion alone remained. A slight dilatation of the retinal veins of the affected eye were the only signs of ocular involvement and vision, and the field of vision were conserved. A rhinological examination by Dr. George B. Wood and an *x*-ray study by Dr. W. F. Manges corroborated the diagnosis of mucocele. With the assistance of Dr. Wood, an incision was made from the inner angle of the orbit, curving under the brow to a corresponding point at the outer canthus. A second incision was also made, which began about 15 mm. above the supra-orbital notch and extended externally in a downward and outward curve, until it joined the termination of the first incision at the outer canthus. This second incision was necessary to permit the elevation of a flap sufficiently large to allow free dissection of the sac which had been exposed by the first incision. As had been surmised, the sac, whose walls were found to be composed of thickened periosteum, was filled with the contents of the greatly enlarged frontal sinus, the bone comprising the anterior wall and floor of the orbit having been entirely eroded

away by the pressure which the slowly distending sinus had exerted upon it. With the escape of the fluid from this cavity, the distended ethmoidal cells came into view. These were thoroughly evacuated and a large opening obtained into the nose. In freeing the superior walls of the sac, great care was necessary, as it was found that the bone in that position had been almost entirely eroded away and that the cavity of the orbit was separated from that of the brain by periosteum only. Tenon's capsule, with its ocular contents, was uninjured by the dissection. Following the evacuation of the fluid, the lining sinus membrane was removed as far as possible and curetted from the posterior sinus wall. The mucocele of the ethmoidal cells was also curetted and a large opening made down to the anterior fossa, sufficiently large to permit the passage of the finger into the nose. The wound was then closed, except at the inner canthus, where an aperture was left sufficiently large to permit of the loose packing of the wound. The orifice of the ethmoidal cells into the nose was kept patulous by a nasal packing. Healing was prompt and without incident. Even at the first dressing, the eye was found to have receded at least a centimeter and the ocular movements had greatly increased in range.

Two weeks after the operation, the exophthalmus had greatly diminished and the excursions of the eye were practically normal.

As might be noted by the second series of photographs, which were taken two weeks after the operation, the wound is entirely closed and in place of the marked prominence over the brow, there is now a pronounced depression. This, however, is rapidly growing less, as the cavity is filling in with new tissue. The excursions of the eye are now practically normal and it is interesting to note that the function of the levator has been practically restored. Uncorrected vision equals $5/7\frac{1}{2}$ in each eye and both fields of vision are normal. There is a hyperphoria of 20°. Dr. Wood reports good drainage from the affected cells into the nose, the anterior ethmoidal cells having been opened after the method of Mosher about a week after the primary operation and the anterior end of the middle turbinal amputated some days later.

Dr. G. B. Wood stated that the interesting features of this case were its enormous size and the amount of bone destruction without discomfort to the patient; also that there existed in the

FIG. 1.—Before mucocele operation.

ethmoidal region a second mucocele holding over two drams of fluid. As to the etiology of such a condition, it seemed rational to believe that the condition was originally suppurative, and that for some reason the bacteria disappeared, leaving behind a hypersecreting membrane with closure of the orifice. Dr. Wood had

FIG. 2.—After mucocele operation.

demonstrated to his own satisfaction at least that it was possible to have a hypersecreting accessory sinus without the presence of bacteria, and he has under his care such a case, in which the

antrum, although containing mucopus, remained sterile, as proved by numerous bacteriological studies. The next most plausible theory as to the etiology of this condition is that there develops in the mucosa of the sinus a cyst which on growing occupies the whole cavity, and finally by its expansion gives rise to even as extreme a condition as seen in this case.

As to the operative treatment of the case reported by Dr. Posey, Dr. Wood desired to call attention to the fact that although he was able to carry his finger through the nostril up into the frontal sinus cavity, the wound into the nose closed so rapidly that it was found necessary later to destroy the larger ethmoidal cells in order to make permanent internasal drainage certain. The permanent success of the operation he believed depends very largely, if not entirely, upon the maintenance of an opening between the nose and the frontal sinus region, because, while the greater part of the sinus may be obliterated, it is almost impossible to entirely remove the whole of the lining mucosa from such an extensive area as was found in this case.

Results of the O'Connor Operation for Squint

Dr. William Zentmayer exhibited two cases of strabismus operated upon by the O'Connor method. The first case was one of divergent strabismus in an eye with a leukomatous cornea. The patient was an adult. The angle of squint had been a trifle less than 30°. About six weeks after the operation, which had consisted of shortening and advancement of the internus with partial tenotomy of the externus, there was a residual squint of 10°. This case had previously been shown elsewhere. The second case was one of esotropia of 28° in a boy, aged twelve years. H = 4.00 D. This had been corrected and glasses worn for several months. Both externi had been operated upon by the O'Connor method. The opposing muscles had not been tenotomized. Without glasses there was a residual esotropia of 8°. With the glasses there was parallelism of the visual axes.

Dr. Zentmayer exhibited these cases not because the results

were brilliant but because the procedure was a new one and had features which appealed to him. He believed that probably the result was secured not so much by the shortening of the marginal strips of the tendon as by taking the strain off the advanced central tongue and permitting it to unite to the sclera at the point to which it was advanced. The result in the second case would have been better had No. 4 catgut been used instead of No. 3, the largest size available at the time of the operation.

Dr. Posey said that he had performed the operation upon two cases, but his results had been less satisfactory than those obtained by Dr. Zentmayer, largely, he thought, on account of his failure to slip the noose far enough away from the scleral attachment of the muscle. If the operation is as effective as would appear from the cases operated upon by Dr. O'Connor and Dr. Zentmayer, it would prove a great boon to ophthalmic surgeons, permitting of the advancement of the ocular muscles in children at a much younger age than is now possible with other methods which necessitate the introduction of the scleral anchor suture. Dr. Posey said that he made it a rule never to advance a muscle by the old methods in a child under ten years of age, on account of the difficulty and danger in introducing the needle into the sclera of less developed eyes.

Modified Thorington Retinoscope

Dr. George S. Crampton showed a retinoscope which he had designed with a view to making the back of the mirror less difficult to clean. The retinoscope described by Dr. James Thorington, while in other respects an ideal instrument, has the disadvantage that it is difficult to polish the back of the mirror from which a portion of the silvering 2 mm. in diameter has been removed, especially as this small area is generally set in a hole in the metal back about 3 mm. in diameter. It is thus difficult to polish the aperture near the edges and much unnecessary annoyance results from a blurred image. The original instrument having a plane mirror 2 cm. in diameter on a 4 cm. metal disk is modified by

cementing a very thin disk of glass on the back of the mirror with Canada balsam. On account of the protection afforded the silvering by the glass, a large bevelled hole 7 mm. in diameter may be left in the metal back and the 2 mm. sight hole can be readily polished.

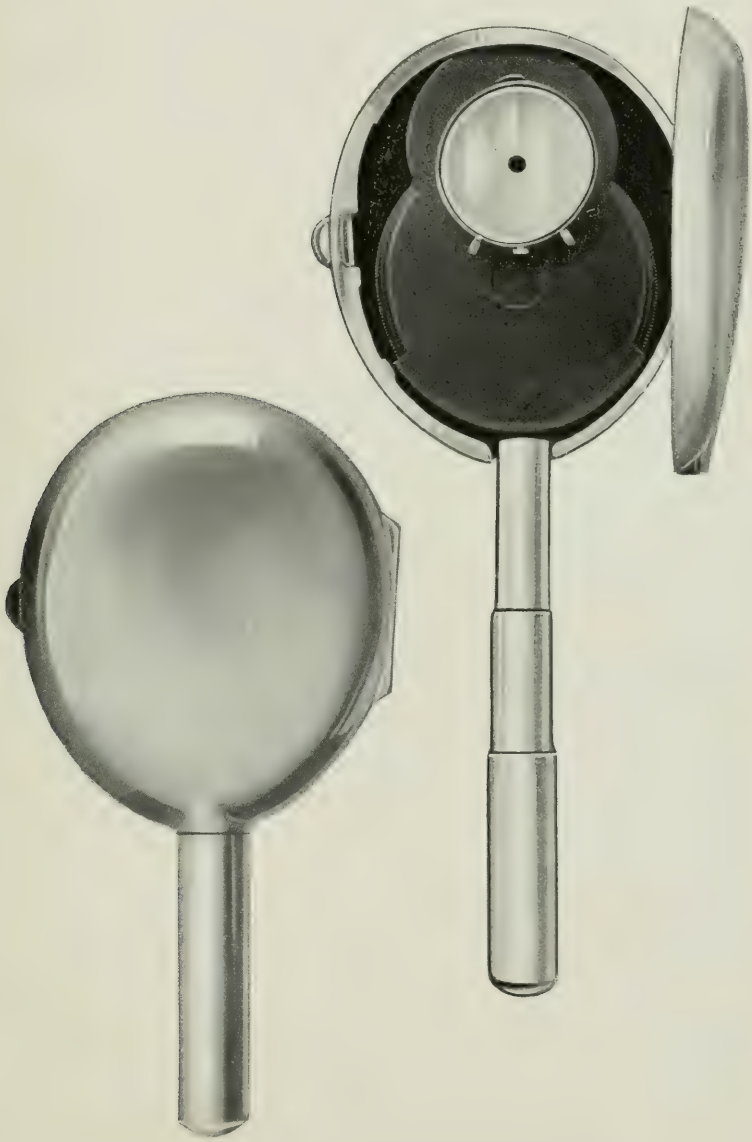
Dr. Crampton called attention to a not uncommon defect found in plane retinoscope mirrors due to uneven polishing or to a bending stress caused by spinning a metal bezel over the edge of the mirror to hold it in place. This defect has been nicely demonstrated by Dr. Lancaster, of Boston, by throwing a beam of sunlight on the ceiling with the mirror. Many of the retinoscopes tested threw a badly distorted image.

Pocket Case for Loring Ophthalmoscope

Dr. George S. Crampton showed a pocket case which he had designed for carrying a Loring ophthalmoscope, the idea being to so reduce the size that it could be comfortably carried in the vest pocket; this was accomplished by using a collapsible handle which when closed extended beyond the case; the latter, stamped from sheet duralumin or German silver, resembled a clam shell or one of the cases recently designed for holding Oxford glasses. An ophthalmoscope with round mirror was found best suited to the case.

Dr. Zentmayer and Dr. Crampton again called attention to the great convenience enjoyed in using their modification of the Loring ophthalmoscope, especially in clinical work where many fundus examinations are made in a limited time.

The revolving disk carries a +16.00 lens between the sight hole and the +1.00; this is accomplished by doing away with the −8.00 and rearranging the lenses. The disk which carries the figures is renumbered on the back. Thus modified the ophthalmoscope was used for years by Dr. Zentmayer before it was independently designed and published by Dr. Crampton.



Pocket case for Loring ophthalmoscope.

Ectatic Macular Coloboma Associated with Choroidal Faults in Periphery of Fundus

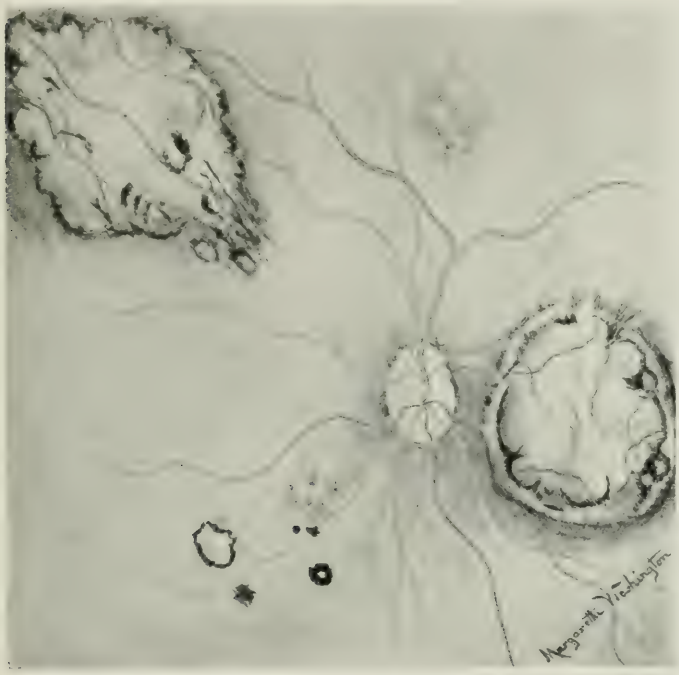
Dr. George S. Crampton described a macular coloboma in the left eye of a girl, aged nineteen years. There was no history of parental consanguinity. Three sisters and two brothers were living and well. One sister was said to have a deviating eye, but as the family lived in a distant city the other members were not examined. The patient was healthy but of a nervous temperament. Aside from moderate divergence of the affected eye, the vision of which was reduced to the counting of fingers at 0.3 m., both eyes appeared externally normal in function and form. In early childhood her parents noticed that she saw poorly with the left eye. The vision of the right eye was 6/6 and its fundus was normal in all respects.

The mediæ of the affected eye were clear and a careful search revealed no other congenital defects than the following: A large, almost round, pearly white, ectatic area about three disk diameters in size occupied the macular region and approached to within half a disk diameter to the temporal side of the nerve. Aside from a slight disturbance of the surrounding pigment, the defect was set in healthy retina but was sharply outlined by a narrow yellowish band which carried an irregular outline of pigment on its inner side. The yellowish circle of concentrated retinal and choroidal elements terminated abruptly and in places even overhung the ectatic mother-of-pearl-colored sack, the depths of which especially in its lower portion measured about 5 D. below the surrounding almost emmetropic fundus. A marked parallax aided in giving an impression of depth.

A branch of the lower temporal artery descended into the deepest part of the coloboma and disappeared. Smaller branches from the upper temporal artery did likewise, and still other vessels, probably choroidal in origin, traversed the floor after springing from the deepest part of the sac.

In the extreme upper nasal periphery of the fundus, another large, lozenge-shaped defect, slightly greater in area than the

macular one, was seen to have a rather scalloped, pigmented outline touched slightly with yellow. The surface of the fault was pearl-gray in color and showed no parallax or other evidence of being ectatic. This area was distant 4 or 5 D. from the disk, and was traversed by a branch of the upper nasal artery. Other vessels crossed the pale area from side to side in a direction



Ectatic macular coloboma.

axial to the disk. One appeared to spring from a mass of pigment on the side next to the disk and extended radially toward the more peripheral side where it proceeded beyond the fault into normal retina.

Some distance from the disk in the lower nasal fundus there was a group of three or four small, pigmented defects. One which was one-fifth the area of the disk showed choroidal vessels traversing a white ground framed in black.

The disk was vertically oval and sharply defined. The side facing the macular coloboma showed a small, decidedly atrophic sector. The retinal vessels were normal in caliber and distribution and the eye was practically emmetropic. The refraction of the good eye was -0.25 sph. $= +1.00$ cyl. ax. $90° = 6/5$.

Colobomata of the macular region or in fact anywhere in the fundus, except directly downward or downward and slightly inward from the disk, are spoken of as atypical, in that they cannot be accounted for by assuming a faulty closure of the fetal cleft. Owing to the fact that atypical colobomata, while having the characteristics of those found in the region of the cleft, could not be accounted for in the usual way, the question naturally arose as to whether or not the faulty closure of the cleft had anything to do with the etiology of the typical type, and Ginsburg took the extreme view that colobomata could only be explained by a theory which excluded the fetal fissure.

Much has been written on the subject and many theories advanced, but as time passes each theory has been shown to have weak points and the question seems to be far from solved. Most observers have sought for a solution which will account for both typical and atypical faults. It is probable, however, that we will have to be content to fit different theories to different types.

Manz, considering only the factors causing typical defects, drew attention to the defective closure of the fetal cleft, from whatever cause, and studied the abnormal development of the surrounding mesoblast which finally becomes differentiated into the choroid and sclera. He also considered the effect of the intra-ocular pressure in causing an ectasia in the cicatricial-like tissue closing the cleft.

While well enough as an explanation of typical defects, these views failed to go further and for a time Deutschmann had many followers in his inflammatory theory which seemed especially suited to an explanation of the macular colobomata. Unfortunately for this theory, histologic study failed to demonstrate any evidence of inflammation in the eyes of the newborn. Furthermore, bilateral colobomata and the finding of defects in several

generations lead one to hesitate in putting full faith in this theory. It is well known that eyes having congenital defects are especially prone to undergo inflammation as they mature. This may account for certain scattered areas of degeneration that are occasionally seen in fundi, the seat of colobomata that in themselves do not have the appearance of having undergone much, if any, inflammatory change.

So little is known of the after-effects which may be expected to follow early inflammation in the fetus that it will always be difficult to say when the damage was done. Leber drew attention to the possibility of the total disappearance of the effects of early inflammation such as sometimes occurs in early postnatal life. Whether developmental anomalies would result would depend upon the stage in which the inflammation occurred.

Pagenstecher studied the effects of toxines circulating in the maternal blood, such as those of tuberculosis and syphilis, and by feeding naphthalin to animals was able to produce colobomata in their offspring. When the poison was stopped normal offspring resulted.

JANUARY 21

Aniridia with Interesting Family History

Dr. S. D. Risley presented a patient with aniridia and a family history extending through four generations. In the first generation John X. had no iris in either eye, his wife's eyes being normal; the condition of his parents' eyes was not known. From him there were 117 descendants, the patient belonging in the third generation. Of these 117 the iris was known to be absent in all except five individuals, in whom the condition of the eyes could not be traced. In two eyes the lens was cataractous, but whether the iris was present or not could not be determined. In presenting the case history Dr. Risley remarked that he had brought it for-

ward as the most remarkable illustration within his knowledge of the persistence of an hereditary anatomical anomaly.

Dr. Holloway stated that he had occasion to make a cursory examination of the literature relating to aniridia at the time he reported the history of his patient before this section some two years ago. As far as he was aware the history reported by Dr. Risley was unique and most extraordinary. Since that time certain information had come to him making it probable that other members of his patient's family had seriously defective eyes, but he had not been able to secure definite data concerning the actual conditions.

Dr. Langdon stated that one very interesting thing about the genealogy reported by Dr. Risley was the very large percentage of affected individuals, greater possibly than Mendel's calculation for even a dominant strain.

Dr. Posey stated that he thought the occurrence of aniridia in so many of Dr. Risley's cases most unusual, for generally there is a transmission of various forms of anomalies of the iris. He referred to two cases which he had shown before the Section some years ago, in which there were double coloboma of the iris and choroids in the eyes of the mother and of the suggestion of a colobomatous-shaped pupil in the right eye and a moderate degree of corectopia in the left in the daughter. He showed the illustrations of a series of unusual congenital defects of the iris, which he had reported in 1897. These ranged from instances of partial aniridia to slit-shaped pupils, like those occurring in cats' eyes. Dr. Posey said the microscopic examination had shown that the root of the iris was present in nearly all cases of aniridia, and that this accounted for the glaucoma which was not infrequent in aniridia, also for the conservation of the act of accommodation.

Dr. Posey referred to an hypothesis which he had advanced to explain the anomalous condition of the iris, by the improper development of its vascular framework. He said that the marginal portion of the secondary optic vesicle from which the iris springs is essentially a vascular tissue, consisting of but little more than a network of bloodvessels, supported on a delicate

connective tissue, which is derived from the endothelial layer and a few spindle cells from the anterior layer. The vessels are formed through the union of the long and anterior ciliary arteries, which anastomose to form the major circle of the iris. From this circle small branches are given off which run inwardly between the cornea and the lens, and represent the chief bloodvessels of the iris. Each of these vascular loops is surrounded with connective-tissue cells which become the stroma of the iris. By this theory the close phylogenetic relationship between coloboma and other anomalous conditions of the iris can be readily explained, a complete typical coloboma representing the absence of a main iridal branch; corectopia, a slight irregularity in the proper distribution of one of the twigs.

Dr. Zentmayer asked Dr. Risley what proportion of the cases had associated anomalies in development such as supernumerary digits or tragi. In regard to the embryologic defect which produces this anomaly he said that the view advanced by Collins and Mayou to explain choroidaremia and macular coloboma was similar to the one suggested by the Chairman to explain anomalies in the development of the iris.

Dr. Hansell: I believe that no previous published example of the transmission of anatomical anomalies can be comparable with that of Dr. Risley's in the number of individuals affected. It is truly most remarkable. It demonstrates forcibly the powerful influence of the heredity of anatomical peculiarities. The trend of modern thought concerning the heredity of disease is along exactly opposite lines. As an illustration I mention the case of a boy, two years old, at present under my observation, who has glioma of both retinas. The father and mother are alive and well. The grandparents, with the exception of one who died of typhoid fever, are alive and free from cancer of any kind. In this case heredity may be safely excluded from the etiology.

Dr. Risley's investigations are remarkable in that they show, as has been pointed out by the Chairman, that the descendants inherited exactly the same anomaly of their progenitors and not a variation from or modification of it.

Modified inheritance is, I believe, more common. For instance, in a family under my observation the mother has coloboma of the iris in one eye. She has seven children, of whom five have double congenital (lamellar) cataracts.

In closing the discussion Dr. Risley said that he had been at a loss for any satisfactory explanation for this striking hereditary anomaly. Speculation, he felt, was fruitless, since it led into the most intricate problems in the science of embryology. He could conceive it possible that an anomaly of the blood supply might furnish an explanation. For example, the absence of the bloodvessels, which later became the long anterior ciliary arteries, would prevent the growth of that portion of the mesoderm and ectoderm from which the iris was developed, and pressed forward with its growth into the anterior chamber between the fourth or fifth months of embryologic life, the choroid and ciliary region being nourished by the posterior ciliary vessels; but he recognized the fact that this was merely speculation. Von Ammen had suggested that the crystalline lens may have been detained too long in its contact with the cornea and so crowded out the tissues from which the iris is formed; but this also was mere speculation.

Two Cases of Monocular Neuroretinitis

Dr. Howard F. Hansell exhibited two girls, seventeen and fifteen years of age respectively, and in neither could the etiology be satisfactorily determined. Physical examination, including the Wassermann and von Pirquet tests and radiographs, disclosed no lesion of the sinuses or indeed of any part of the body. The presence of acute infection or toxemia could not be demonstrated. In one case, associated with the edema of the nerve head, was the clearly marked, star-shaped figure in the macula suggestive of nephritis. Many chemical and microscopic analyses of the urine were made and all were lacking in special indications. In this patient "yellow vision" was a conspicuous symptom. Under

mercurial inunctions, daily sweat baths and potassium iodide the macular figure disappeared, the edema of the papilla decidedly lessened, and vision became nearly normal.

In the other patient marked improvement followed a course of similar treatment. By continued observation and study the etiology may be made plain.

Dr. Risley said he had been greatly interested in these carefully reported cases of Dr. Hansell's. He had himself seen three cases of monocular neuroretinitis in which there was marked retinal edema concealing or obscuring all details of the fundus. Two of these he had already reported at the College several years ago, the third had occurred within the past year. In one of the early cases the edema had come on suddenly. A woman, a Wills Hospital patient, had been ironing in a very hot room and had stepped to the door of the laundry, with her head and face exposed to the bright sunlight and draft in the doorway, when her vision suddenly became blurred. There was no red spot at the macula. The case recovered normal vision under the use of iodide of potassium. In the third case, a private patient who was in bad general health and had been under treatment from time to time for headache, apparently due to eye-strain, woke up in the morning, after a restless night, with blurred vision in her left eye. Vision was found reduced to 6/30 and there was an extensive retinal edema most marked in the nasal half, the inner border of the nerve being quite concealed, the temporal half of the eye-ground being fairly normal. In the centre of the edematous area a more densely white spot could be seen with the electric ophthalmoscope, which suggested the possibility of a local infection. A von Pirquet test proved very positive, and under slowly ascending injections of old tuberculin the edema rapidly subsided, vision rose to normal acuity, and her general health rapidly improved. Dr. Risley thought, therefore, that in cases of monocular neuroretinitis careful search should be made for general toxemias and local specific infections. He had often seen moderate degrees of edema worse in one eye than in the other, or practically entirely absent in one and with relative or absolute central scotomata

associated with intestinal infections or disease of the sinuses contiguous to the orbit.

Dr. Holloway stated that during the past year three cases of unilateral choked disk had come under his observation. In two of these cases no positive etiologic factor had been determined. Both of these had been thoroughly studied at the University Hospital. While small doses of iodides had been administered for a time, its use had not been persisted in. In both instances there was recovery with normal vision. During the past week, however, one of these cases had again come under observation, complaining of severe headaches and with probable recurrence of the choked disk, the other eye remaining normal. The third case was of specific origin, probably dependent on the so-called gummatous meningitis; after the use of salvarsan both by the intraspinal and intravenous methods, associated with mercury and iodides by the mouth, the condition subsided with full visual acuity.

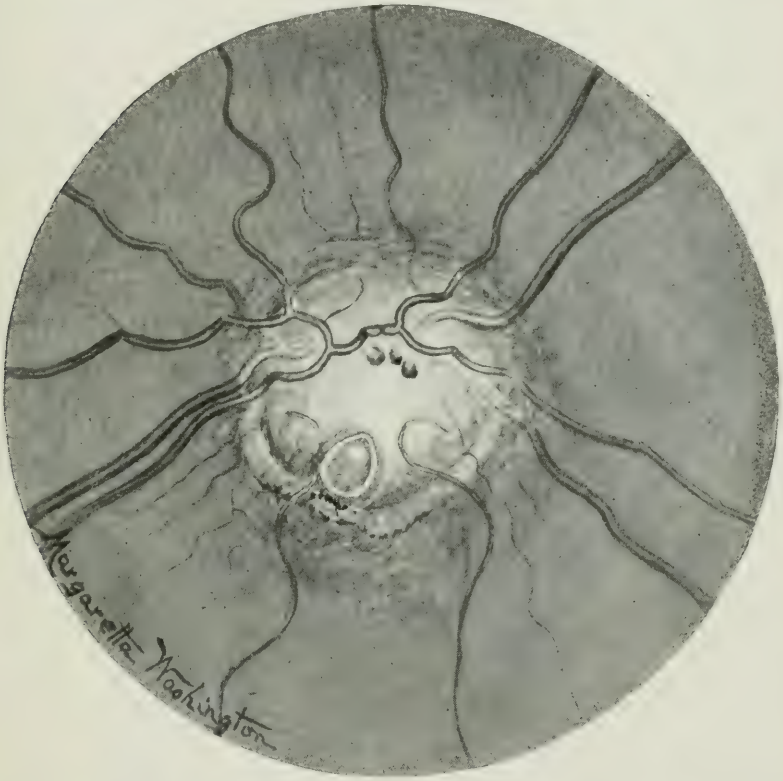
Dr. Posey recalled to the Section two cases of monocular neuroretinitis of high degree in young girls, in whom the only causal factor seemed to be a moderate degree of chlorosis. The vision in both improved rapidly under administrations of iron.

Crater-like Hole in the Disk Associated with Pulse-like Movement of an Overlying Membrane

Dr. T. B. Holloway referred to a male, aged nineteen years, who had come under his observation at the University Hospital. Aside from the condition about to be described the eyes were normal, and with the correction of a low hyperopic astigmatism normal vision was obtained.

Situated in the lower outer quadrant of the left disk was an egg-shaped pigmented area with its long axis corresponding to the long axis of the disk. The periphery of the lesion corresponded to the margin of the disk, and in size was about one-third the diameter of the papilla. The lesion was greenish-black in color. It conveyed the impression of an excavation, as one could distin-

guish a sloping of the margins to the position of a white rim lying just within the periphery. In attempting to determine the depth of the supposed excavation careful examination detected the pulsation of a small milky area situated somewhat eccentrically up and in from the centre of the lesion. The direction of the



Crater-like hole in the disk associated with pulse-like movement of an overlying membrane.

pulsation was in the long axis of the hole. At a subsequent and more careful examination with suitable manipulation of the light a faint pulsation could be detected over practically the whole membrane.

After referring to the literature of the subject, and especially

to articles by Coats and Reis, Dr. Holloway stated that he believed the pulse-like phenomenon was brought about by a pulsation transmitted by the central vessels to the overlying membrane, and while the presence of fluid would not be essential to the development of this phenomenon, its presence would seem to facilitate its production. As far as he was aware, in none of the patients whose histories had been previously recorded had this pulse-like phenomenon been observed.

Dr. Krauss stated that he had recently examined a patient who had a hole in the optic disk with a small vessel running across its floor. The patient was a woman, aged fifty-nine years, who came to him for refraction. Her vision with the assistance of convex spherocylinders was normal in both eyes. The fundus of the left eye was normal with the exception of marked tortuosity of the vessels. In the right eye the disk showed an eccentric excavation at the outer side with marked tortuosity of the vessels. Near the lower outer side of the disk there was a round greenish mark about $\frac{1}{8}$ disk diameter in size, which on focussing was seen to be a deep excavation, upon the floor of which there was a cilioretinal vessel which disappeared at both sides of the cavity. The retinal vessels were seen with a +2.00 D. lens while those in the bottom of the hole were seen with a −4.00 D.

Rupture of Sclera with Dislocation of Lens into Episcleral Tissues

Dr. Frederick Krauss described a case of rupture of the sclera with dislocation of the lens into the episcleral tissues. The eye had been struck by a fist ten days before, but was neglected on account of the absence of pain. There was an enormous staphyloma, directly above and extending about 5 mm. to the nasal side of the cornea, and about 18 mm. backward. A purse-string suture was placed about the staphyloma in the deep episcleral tissues, with the opening of the suture posteriorly. An incision was made through the most prominent part, just posterior to the usual position of the ciliary body, extending through the conjunctiva

and dense episcleral tissue. Clear lens matter exuded to the volume of a normal lens. No vitreous or hemorrhagic extravasation complicated matters. The suture was drawn tightly and was guarded by a second suture to close the wound more securely. The eye was doing well, hand movements being seen twelve days after operation. The vitreous was still filled with blood, and a broad coloboma occupied the upper third of the iris.

Concerning the Motais Operation for Ptosis

Dr. Charles R. Heed reviewed briefly the Motais operation and reported three cases operated upon within the past year. The original procedure of Motais was followed in the first two cases, while in the third the modification as suggested by Dr. H. D. Bruns, of New Orleans, was carried out. The results in all three cases were considered very satisfactory. The original method proved quite as effective and the procedure less complicated than the modified form.

The advantages claimed for the operation were:

Absence of a visible scar;

The synchronous movement of the lid with the globe;

Absence of a scowl or wrinkling of the forehead; and

Close apposition of the lid and globe.

Dr. Shoemaker referred to a Motais operation which he had recently performed, in which the little tongue of rectus muscle became detached after several days and remained in the lid. The operation was of course a total failure. Upon the fellow-eye he subsequently operated after the method of Hess and secured an excellent result.

While the Motais operation if successfully executed gives the most perfect and beautiful results, Dr. Shoemaker believes that for him at least it is very difficult and uncertain, and permits of no later interference in the interests of a more satisfactory final result.

He will, however, continue to employ the operation in suitable cases, with the hope of overcoming the difficulties and uncertainties.

Dr. Zentmayer said that he had had but little experience with the Motais operation, but thought that one of Dr. Shoemaker's objections might be overcome by the use of a stay suture passed about the levator and brought out through the lid as in Eversbusch's operation for ptosis, as suggested by Wilder. The procedure is designed to take the tension off the small tendinous tongue during the healing period.

Dr. Sweet stated that he had not been aware that Motais brought the tongue of muscle anterior to the fornix in attaching it to the tarsus until Dr. Heed called his attention to the author's description of the operation. Dr. Sweet said that in the limited experience he had had with the operation he split the muscle as far back as possible and brought the edges of the conjunctiva over the separated portion.

Operative Results in Extensive Anterior Synechia

Dr. G. Oram Ring exhibited a girl, aged twelve years, showing the operative result in an extensive anterior synechia.

The child when six months of age was cut in the right eye with a piece of glass, the cornea being severed from the upper corneoscleral margin to a point slightly below the corneal pole.

The process of healing induced a dense white cicatrix, 8 by $1\frac{1}{2}$ mm. in size, to the entire length of which the iris was firmly bound, the lower portion of the iris being drawn up from below, leaving only a 1 mm. eccentrically placed pupil down and slightly in.

The marked stretching of the iris fibers, with the danger of subsequent atrophy, the pull upon the ciliary processes, and the cosmetic need in a very attractive, growing girl, suggested an incision of the iris along the area of adhesion. This was

accomplished by the careful introduction of a narrow Graefe knife, which was carried to the summit of the cornea, entirely severing the iris attachment, with a most gratifying result, the iris receded to a correct position, being only slightly narrowed above, and its appearance closely approximated that of the normal eye.

Extensive Emphysema following Wound of Lacrimal Canal

Dr. George S. Crampton exhibited a man, aged thirty-three years, in whom a slap on the face by a man's open hand was followed by an extensive emphysema extending to the point of the shoulder.

The patient was struck on the right side of the face and applied for treatment at the Pennsylvania Hospital on account of the swelling, which, beginning with a mere puffiness of the lids the night of the injury, assumed what to him seemed alarming proportions the next day following his efforts to dislodge some blood-clots by forcibly blowing his nose.

The air penetrated the subcutaneous tissues on the right side of the face and neck, extending as far as the point of the right shoulder and the clavicular region below. The crepitating area extended anteriorly across the neck and could be felt as far as the outer extremity of the left clavicle. There was no extension on the face beyond the median line, nor above the eyebrows on the affected side. Pressure on the lower lid caused the air to pass freely into the upper lid but there was no evidence of air in the orbit. The eyeball was not injured and retained its usual position. The nasal bone was said to have been fractured in childhood but an *x*-ray failed to show any old or recent fractures and the sinuses, although extremely large, did not appear to be broken.

There was no external evidence of the location of the injury, neither was there laceration of the skin or subcutaneous ecchymosis. However, the fact that the orbit was not affected in spite of the extensive emphysema of the face, pointed to a rupture external

to the orbit. Fuchs states that a purely palpebral emphysema without implication of the orbit is extremely rare and occurs when the point at which the air enters the tissues lies in front of the septum orbitale, *e. g.*, in injury of the lacrimal sac.

When the air enters behind the septum orbitale the lids are squeezed together and the fissure is narrowed, while in other kinds of proptosis the lids are pressed apart by the eye. When the air breaks through the orbital fascia and enters the lids it can be much more easily felt than when it is behind that tightly stretched tissue which is attached to the convex border of the tarsus and prevents the air reaching the free border of the lids.

Heerfordt, in discussing a case of emphysema of the orbit, stated that it is often caused by a trivial injury; others believe the mere forcible blowing of the nose is sufficient in persons having a delicate lamina papyracea to cause an opening into the pneumatic cavity and consequent emphysema.

Dr. Posey said that while emphysematous conditions about the eye usually disappear without leaving sequelæ, this was not always the case, and referred to a patient who developed a chronic inflammatory tumor with cyst and giant-cell formation in the floor of the orbit, and connected with the lacrimal sac, which arose after the false passage of lacrimal probes. The operation had been performed by another surgeon some months before Dr. Posey saw the case, but the patient claimed that there had been marked swelling and discoloration of the lids by the blood which invaded the tissues under the skin after the probing. Later on a swelling appeared at the inner angle of the eye, which disappeared on firm pressure, but this phenomenon was attended by a peculiar crackling sensation. The swelling was larger in the morning and also after exercise. Blowing the nose did not increase its volume. The growth slowly increasing in size and causing some disfigurement, Dr. Posey excised it, and found it to consist of a mass of newly formed tissue, the surface of which was studded with numerous small cyst-like elevations which crackled under the finger. No distinct capsule could be defined.

Histologic examination showed a fibrotic stroma with occasional small collections of lymphocytes, and scattered through it were numerous small cysts varying in size and without contents. The specimen was not a true tumor, but the reaction of tissue to some form of foreign-body irritation. The air doubtless entered the tissues in the region of the sac through a small fissure in the inner orbital wall, in consequence of the false passage of the probe.

"Drusen" of the Choroid

Dr. H. Maxwell Langdon exhibited a woman, aged fifty-three years, who applied at the Orthopædic Hospital, in the clinic of Dr. Morris J. Lewis, complaining of a weakness of the left leg. An inequality of the pupils was noted and an ophthalmic examination was requested.

Central corrected vision was normal, the right pupil was slightly larger than the left, but their reactions were normal and prompt. Ocular rotations were full and equal, the media were clear, and the disks and fundi normal, except for a large patch of "Drusen" in the left eye, to the nasal side of, and slightly lower than, the disk. It was about twice the size of the papillæ, and was distinctly elevated above the fundus level, which was +1.00 D. The highest point of the hyaline patch was about +3.00 D; it was glistening, especially the lower margin, where there were numerous small star-like particles which shone brilliantly in the reflected light of the ophthalmoscope. It had the appearance of being arranged in layers, one on the other, the surface being quite irregular and wavy. There was a corresponding absolute scotoma in the temporal portion of the visual field. It was the largest single patch Dr. Langdon had seen.

Dr. Posey said that he had never seen such a large group of colloid matter except in one case, when the deposit was on the head of the optic nerve.

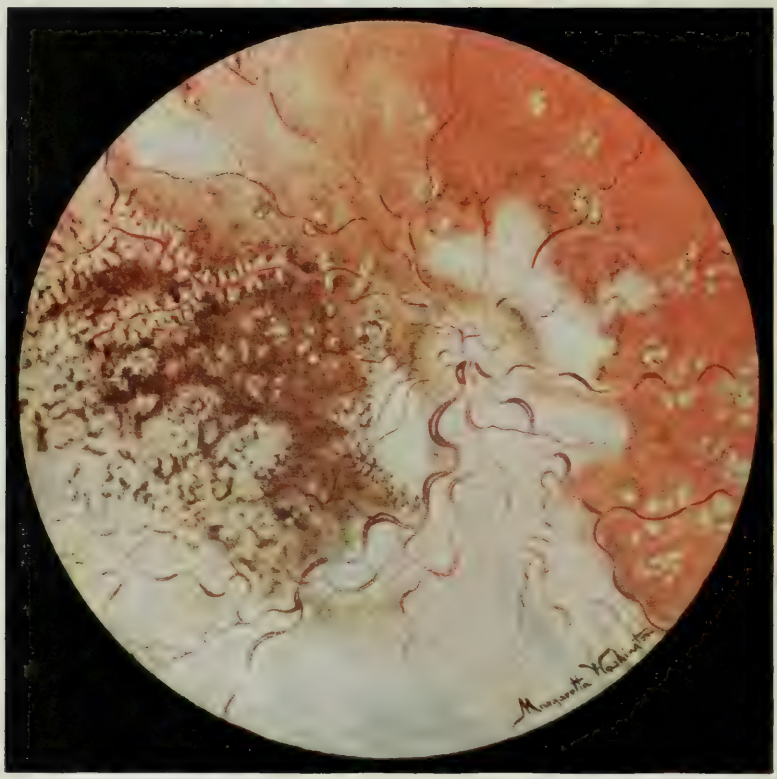
FEBRUARY 18

Dermoid Tumor of Inner Angle of Orbit Resembling Deformity Caused by Mucocele of Ethmoid Cells

Dr. William Campbell Posey showed a case upon which he had recently operated for the removal of a dermoid tumor from the inner part of the right orbit. The point of interest was the resemblance of the case to one of mucocele of the ethmoidal cells. A photograph was exhibited, taken prior to the operation, which showed this similarity very clearly.

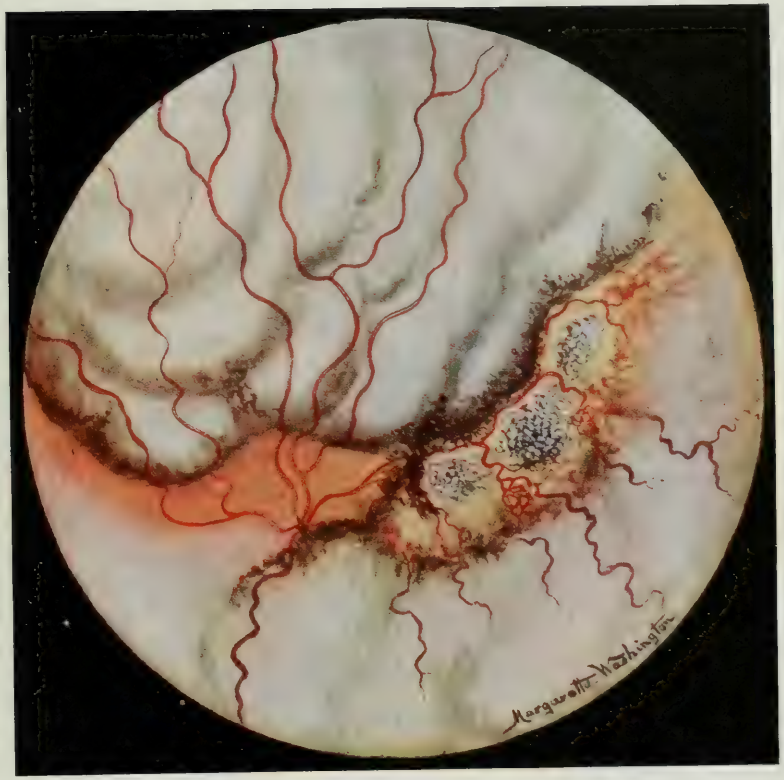
Traumatic Enophthalmos

Dr. Howard F. Hansell exhibited a man who was struck in the left forehead and orbit by a horse's hoof. The frontal bone was fractured and depressed and the brain protruded. The outer third of the lower margin of the orbit was also crushed and the broken bone removed. He was unconscious and in a precarious state for ten days. Upon recovery he had diplopia and enophthalmos. Three months after the injury vision in both eyes began to fail. In January, 1915, vision of left was reduced to 20/50 and the fields of both eyes were concentrically contracted, that of the left decidedly. The lower outer portion of the orbital margin was sunken and the depressors of the eye partially paralyzed. Under treatment by diaphoresis, mercury and potassium iodide, central vision was restored to normal and the fields doubled in size. The cause of the enophthalmos in this patient was cicatricial contraction of the retrobulbar tissues, absorption of orbital fat and probably paralysis of the unstriped muscle of the anterior orbital fascia. The prognosis is less unfavorable than in those cases in which the optic nerves and the nerves to the muscles are directly compressed by broken orbital walls.



Case 1.—Right eye

Retinal Disease with Massive Exudation



Case 2.—Left eye

Retinal Disease with Massive Exudation

Massive Exudate in Retina

Dr. William Zentmayer exhibited an Italian boy, nine years of age, who stated that four months previous he had first complained to his father of failing vision. His sight was particularly poor in poor light. He went to school and could read up to that time. There was no history of trauma or ear disease. He had measles in a light form when two years old. His mother died in childbirth. Of six children, five died in infancy. Father denied venereal infection. The vision of R. E. = 3/60; L. E. = L.P.: The right pupil was 4 mm. Anterior chamber normal. L. E. Pupil 5 mm., immobile, pupillary pigment border broad. Iris stroma had lost some of its pattern. T. relatively high as compared to R. E., which was a trifle low.

R. E. Vitreous filled with dust-like opacities; the papilla prominent and over capillary. There was an opaque, dense white, prominent mass extending from the region of the ora serrata up to the lower margin of the papilla; from there it swept out past the macular region into the temporal region as far forward as could be seen with the ophthalmoscope. The surface of the mass was undulating, as evidenced by the course of the vessels; its margins did not end abruptly, but merged into the surrounding retina by a broad fringe of small coalescent areas of apparent degeneration, not unlike the changes sometimes seen in advanced albuminuric retinitis of chronic interstitial nephritis with high degree of angiosclerosis. No hemorrhages were visible. There was a second opaque area surrounding the upper margin of the papilla. Scattered throughout the fundus, especially along the course of the vessels, were small areas of degeneration about twice the diameter of the main trunk of the a. c. r. The surface of the exudation was greatly elevated. The inferior artery and veins were greatly distended.

L. E. Almost complete separation of the retina into sagittal lobes. The inferior temporal surface showed hemorrhages and the surface was mottled. Transillumination gave a faint reflex from most parts.

Wassermann and von Pirquet were negative.

T. of R. E.: February 15, 20 mm.; February 16, 20 mm.; February 18, 24 mm.

The O'Connor Operation for Shortening or Advancement of the Ocular Muscles

Dr. William Zentmayer, in reporting a number of cases upon which he had performed the O'Connor operation, described the operative technic as follows: An extensive curvilinear conjunctival incision approximately concentric with the corneal margin is made over the insertion of the tendon. Tenon's capsule is then dissected from the tendon, leaving the latter lying bare upon the sclera. The tip of an iris repositor is inserted into the tendon about 2 mm. from its lower border and passed beneath the tendon and brought out through the tendon 2 mm. from its upper border. It is then slid to and fro so as to separate this intermediate portion of the tendon from the two narrow marginal bands. The portion overlying the blade of the instrument is then clamped in an advancement forceps and the repositor withdrawn. This included tongue is then cut loose close to the scleral attachment of the tendon. It is then reflected, leaving two marginal bands lying upon the sclera. A loop of catgut (Lukens non-chromicized twenty-day) is slipped beneath the lower band and the ends of the gut are passed through the loop and are drawn upon in opposite directions, lengthwise with the tendon. This causes the tendon band to become looped about the gut, thus appreciably shortening it. The gut is then held up by its ends close together and the loop in the tendon-band is lightly ligated close to the tendon with a No. 00 strand of gut. The upper tendon-band is treated in the same way. The middle portion of the tendon and the conjunctiva is then advanced after the manner of the Jackson single-suture operation.

For deviations of more than 15 degrees both muscles are advanced. Tenotomies are not combined, but in some instances are done several months later.

Dr. Posey said that he had been impressed most favorably with the O'Connor method. In several cases he had included the entire upper half of the muscle in one of the loops and the lower

FIGS. 1, 2, AND 3 SHOW THE O'CONNOR METHOD FOR SHORTENING OR ADVANCEMENT OF THE OCULAR MUSCLES AS PERFORMED BY DR. WILLIAM ZENTMAYER.

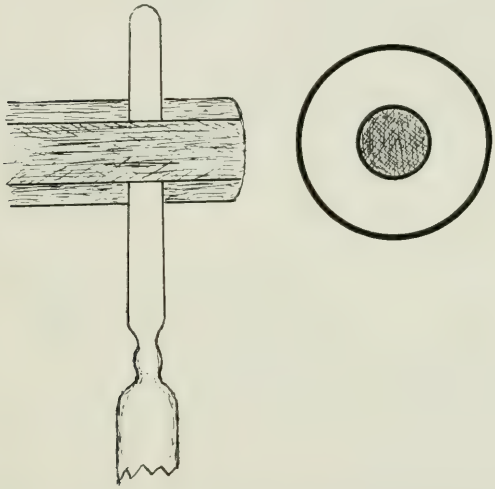


FIG. 1.—Method of separating the marginal bands with an iris repositor.

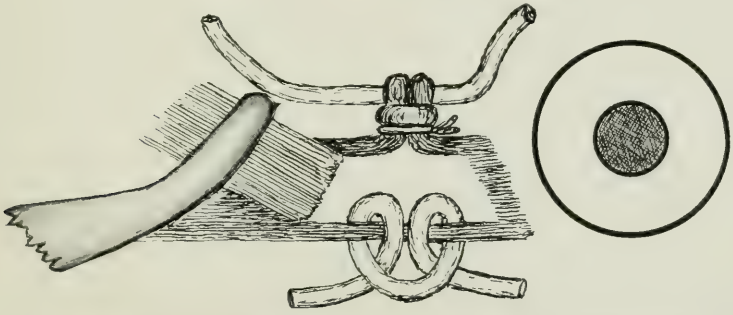


FIG. 2.—Method of throwing the loop from catgut to marginal band of tendon, showing one side shortened and tendon loop lightly held with fine catgut to prevent retransfer of loop from tendon to heavy catgut.

half in another loop, thus doing away with the middle flap. The results, however, had not been entirely satisfactory. He had made this modification on account of the thinness of the muscle which is often present in squint cases and because he had been of the opinion that the middle flap as advanced by the author of the operation had but little to do with the ultimate result.

Dr. Chance said he wished to emphasize particularly Dr. O'Connor's directions as to the manner in which the catgut should be adjusted to the fascicle of tendon. After the ends have been

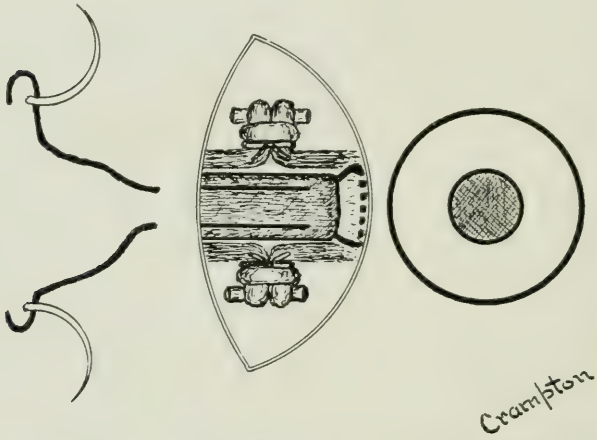


Fig. 3.—Ready for final tie, sutures pass from scleral hold through central tendon-band and conjunctiva. The short bars included in the loops are the remains of the heavy catgut used for throwing the loop onto the tendon-slips.

carried through the loop they must be drawn out parallel to the tendon. The two loops thus formed are then to be carefully drawn together, so as to doubly include the tendinous band. Shortening of the bands cannot occur when the catgut loops are simply hitched on. He had the opportunity of witnessing three operations by Dr. O'Connor, and had seen about ten cases in the hands of other surgeons, with varying results. He thought success depended upon strict attention to the details of the adjustment of the catgut loops

Dr. Schwenk stated that he had two cases at the Wills Hospital upon which he had just done a modified O'Connor operation. The tendons were so small that he split them and tied the two bands with catgut after the manner of O'Connor. He considered the O'Connor operation safe and ingenious.

Sarcoma of Choroid with Cataract

Dr. Peter N. K. Schwenk reported a case of melanosarcoma of the choroid complicated with senile cataract. A man, sixty years of age, came to the Pennsylvania Hospital for the removal of a cataract from his left eye in which he had noticed failing vision for two years, but a more sudden loss within six months, associated with several attacks of headache and a feeling of weight over the left eye and in the occipital region. His ocular condition was as follows: Except for an error of refraction the right eye was normal, while the left showed a mature senile cataract with loss of pupillary reactions. Above the corneal limbus there were two round areas of bluish-black pigmentation about 2 mm. in diameter. To the temporal side there were two engorged, tortuous, lilac-colored vessels. Posterior synechia were present and the tension was plus two. Transillumination on three occasions resulted in a diagnosis of intraocular growth occupying the upper outer quadrant of the globe. *X*-ray findings were negative. The diagnosis was verified on enucleation, which was followed by relief from his symptoms. Dr. Schwenk called attention to the importance of transillumination in cases of this sort which he thought could not be too strongly insisted upon.

Congenital Paralysis of the External Rectus, with Paresis of the Internal Rectus and Retraction Movements of the Eyeball

Dr. J. Milton Griscom exhibited a boy, aged seven years, who was first seen at the Wills Hospital in the service of Dr. S. Lewis Zeigler. During the examination for ocular motility it was

observed that during associated movements of the eyes, when looking to the left, the left eye failed to move outward, and, when the patient was directed to look to the right, the left eye did not perform the movements of adduction, but turned sharply and directly upward, accompanied by a retraction movement of the globe and narrowing of the palpebral fissure. The phenomenon did not occur during monocular fixation with the left eye to the same degree. Dr. Griscom mentioned the collection of these cases made by Duane, who considered the underlying cause of this condition to be a congenital absence of the external rectus or its transformation into a connective-tissue cord. When the eyeball is adducted the retraction is probably due to the fact that the external rectus, being thus inelastic, will not permit inward rotation, and the contraction of the internus causes the globe to recede. Other cases have been reported in which the phenomenon was considered to be due to the fact that the insertion of the internus was too far back, so that when contraction took place the globe was not adducted but retracted.

Annular Opacity—Vossius Ring—of the Lens Following Penetrating Wound into Vitreous

Case I.—G. K. J.—Four hours after the injury Dr. Holloway removed a piece of steel from the right eye of the patient, at the Polyclinic Hospital. The magnet extraction was uncomplicated, the piece of steel weighing 1.5 decigrams. The foreign body perforated the upper lid 13 mm. above the margin, entered the vitreous chamber through a scleral wound 2 to 3 mm. in length that was situated slightly up and out 9 mm. from the limbus of the cornea. At the time of examination the vitreous was much clouded and showed a number of streak-like hemorrhages from the direction of the wound. The vision was reduced to counting fingers at eighteen inches. Seven days later, when next examined by Dr. Holloway, a low-grade cyclitis had developed and in the lens could be noted a typical Vossius ring associated with a number of large central geometric opacities, but these were not dense.

Four days later all the larger opacities had disappeared and the ring was less preceptible. By three and a half weeks after the injury no trace of the annular opacity could be seen. Seven weeks after the accident the vision was 6/12.

Case II.—A boy, aged twelve years, was admitted to Dr. de Schweinitz's service at the University Hospital with a history of having been struck in the left eye with a B. B. shot. On admission the vision was reduced to hand movements at one meter. There was some blood in the anterior chamber, two small tears in the ciliary margin of the iris up and out; the vitreous was much clouded. Ten days later, when first seen by Dr. Holloway, there was a typical Vossius ring evidently in the subsiding stage. Up and out in the lens was a sector-like opacity in the posterior layers. Some edema about the posterior pole was still visible while a small patch of retino-choroidal disturbance could be vaguely seen showing through the edematous areas in the region between the disk and macula. Three weeks later the Vossius ring had entirely disappeared. Four months after the accident the vision of the right eye was 6/7.5. The sector-like defect in the lens has remained.

Dr. Zentmayer said that he had before recorded having seen a case of ring cataract which had led him to believe that this opacity might be permanent. In the notes taken at the time of the injury such an opacity had been noted as present in an eye following a trauma. Ten years later upon reëxamination it was still present. He had considered that probably a degeneration of the anterior capsular cells had occurred.

Metastatic Gonorrheal Iritis

Dr. George S. Crampton reported a case of metastatic gonorrheal iritis in a man, aged twenty-nine years, who had had a single attack of gonorrheal urethritis three years before his iritis came on.

His urethritis was not especially severe or prolonged and apparently he made a complete recovery. He had no symptoms pointing to the affection for three years or until three months ago,

when he was troubled with frequent micturition. There was trivial hematuria but generally the urine was clear. There was no pus at any time and the condition was not associated with his almost forgotten urethritis.

Six weeks ago he had a slight phlebitis of the left leg, followed by pains in the lumbar region, which in turn passed to the right shoulder, and then to the right eye which became deeply injected and sensitive to light. Shortly afterward he made his appearance at the eye clinic of the Pennsylvania Hospital. The bulbar conjunctiva of the left eye was more generally injected than is usually the case in iritis, there being but little increase in the intensity of the redness in the pericorneal zone. This peculiarity, together with the irregular dilatation of the pupil after the instillation of atropin, attracted especial attention, and his history was carefully gone into. He was put in bed for a few days, and his prostate was stripped and yielded Gram negative intracellular gonococci.

A gonorrheal complement-fixation test was positive and his Wassermann was negative. The treatment consisted of formin in five-grain doses fourth hour to combat the cystitis, together with atropin and dionin locally.

Both the cystitis and iritis yielded in three weeks, and he was referred back to his physician in another city for further attention.

Dr. Shumway asked Dr. Crampton if he had considered using injections of gonococcal vaccines or serum in his case, and reminded the Section members of the case of gonorrheal iritis which he had reported before the Section in 1910, from the wards of the Philadelphia General Hospital. There had been multiple joint involvement also in the case, and the conditions had resisted ordinary treatment. Three injections of gonorrheal vaccine had been followed by almost immediate subsidence of both the iritis and arthritis.

Dr. Zentmayer asked Dr. Shumway what dosage he had used. There was a difference of opinion among clinicians as to the proper dose. Some, as Weeks, employed small doses, while others, Cole and Meakins, for example, used very large doses.

In response to Dr. Zentmayer's question, Dr. Shumway said

that doses of 100,000,000 dead organisms had been employed in his case. He knew that many of the American observers had considered 50,000,000 a large enough dose, but he had felt that in the absence of any untoward reaction the larger dosage was advisable in order to get as prompt results as possible.

Dr. Holloway referred to a patient who had come under his observation at the University Hospital with an intense spongy iritis that had been preceded for a week by episcleritis. He had an extensive joint involvement and after prostatic massage gonococci were found. His last acute attack had been a year before. Owing to slight delay in securing vaccines some improvement had already occurred before their use. Doses of 100,000,000 were given and the eye made a very prompt and thoroughly satisfactory recovery.

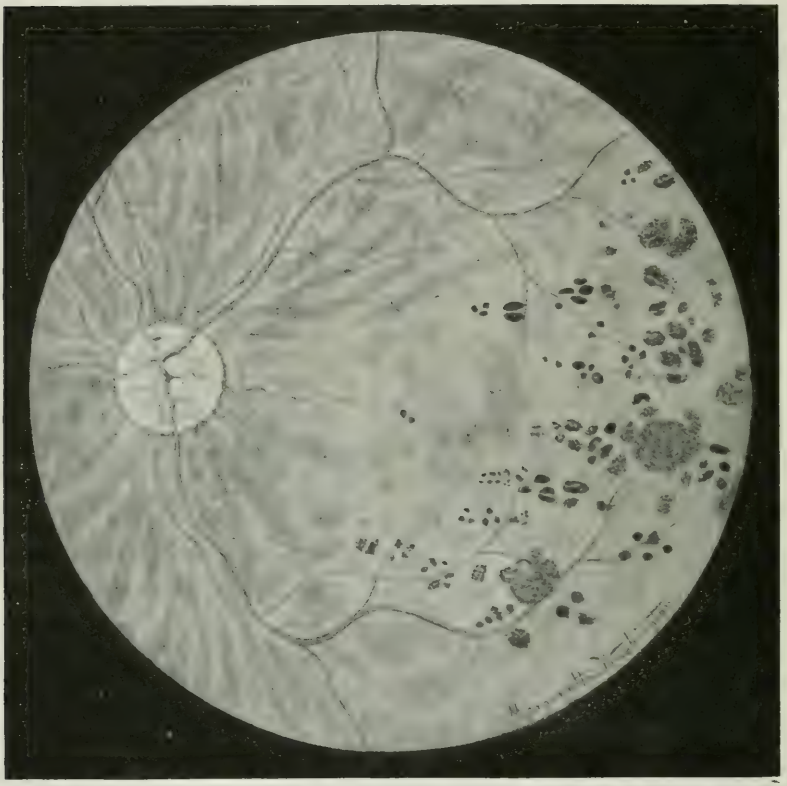
In reply to Dr. Shumway's question, Dr. Crampton stated that while the use of gonococcal vaccines had been considered, the recovery of the patient had been so prompt that they were not resorted to.

MARCH 18

A Peculiar Form of Retinal Pigmentation

Dr. Burton Chance gave an account of two examples of a peculiar form of retinal pigmentation, of the form described by Stephenson in 1891. Chance found his first case in a boy of ten, and the second in a young man who had had an injury of the fellow-eye following a coasting accident. In the boy's eye the pigment areas were scattered well over, and extended far forward, in the superior nasal quadrant. They occupied the midtemporal section in the second case, as shown by a drawing exhibited. The spots were chocolate brown in color, of various sizes and polyhedral in shape, arranged in groups or rosettes, chains or like diplococci. A few spots lay on the vessels, but most of them lay beneath. There were no signs of inflammation or of atrophy

in the eye of either case. The pigmentations are assumed to be congenital in their origin, and not a form of pigmentary degeneration, as Jaeger thought a case he had had might have been.



A peculiar form of retinal pigmentation. (Dr. Burton Chance.)

A Case of Atypical Pigmentation of the Retina

Dr. Zentmayer said that his case presented no features essentially different from those detailed by Dr. Chance. The left eye was the one affected. The pigment dots were confined to the middle nasal sector of the fundus. The vascular supply was also anomalous, inasmuch as the larger vessels were distributed to

the nasal portion of the fundus. An interesting point is that the pigment in these cases is often chocolate brown in color, the same as the pigment in "angioid streaks" in the retina, a point against a hemic origin of the latter.

Dr. Zentmayer in closing. Just a word as to the explanation of this anomaly: According to Collins and Mayou it arises from adhesion of the two layers of the secondary optic vesicle. These authors state that a microscopic study of the condition has been made, showing that the pigmented cells surround small hyaline nodes, probably the product of secretion of these cells.

Congenital Pigmentation of Retina in Association with Anomalous Distribution of Retinal Vessels

Dr. George S. Crampton exhibited a woman, aged forty-five years, who applied at the Pennsylvania Hospital for the removal of a small chalazion. Externally the appearance of both eyes was normal, as was also the fundus of the left eye. The vision of R. E. = 6/6 and of L. E. = 6/20. The mediæ of the right eye were clear and the fundus appeared normal except for an anomalous distribution of the retinal vessels and the presence of a number of small, sharply defined, round or biscuit-shaped spots of black pigment. These spots, sometimes in pairs like large gonococci and again in groups of three or more, extended from a point two disk diameters from the disk into the extreme periphery of the fundus along the course of the upper nasal vessels. In no instance did the spots overlie the vessels, but an arterial twig was seen to pass over two of the spots. The disk was the seat of a large central excavation with slightly undermined edges. There was a small spot of pigment on the upper nasal margin which differed in appearance from the other spots.

These spots, as shown in the cut, have the same general appearance as those in the cases described by Dr. Zentmayer and Dr. Chance.

Dr. Posey said that in 1893 a case of pigmentation of the retina similar to those described came under his notice, which was of

peculiar interest by reason of the fact that it was the first fundus sketched by Miss Margaretta Washington. The pigmentation occurred in a girl, about sixteen years of age, and was grouped chiefly about the lower temporal vein of the right eye.

Congenital pigmentation of retina in association with anomalous distribution of retinal vessels. (Dr. Crampton.)

Bilateral Glioma of the Retina

Dr. Howard F. Hansell reported a case of bilateral glioma of the retina; the tumor in the left eye had advanced to the second or glaucomatous stage. The boy, aged two years, was weak and irritable, and, according to the parents, was losing ground every day. A white, shining, rounded growth, of the apparent size of a pea, projected into the vitreous from the retina just to the temporal side of the nerve in the *right* eye. In the periphery of the field vision was fairly good—in the centre he could see nothing. After enucleation of the left, recovery was prompt and the health rapidly improved. Three weeks later second examination of the right showed decided increase in the size of the glioma. Microscopic examination of the enucleated left bulb confirmed the diagnosis of glioma. The parents were instructed as to the

nature of the disease, and were advised to have the right ball enucleated as soon as the eye should be blind.

In the bilateral cases, which constitute about 25 per cent. of the total number, the disease appears in one eye, the second being involved some months later. The question arises, Would prompt enucleation save the second eye? The four cases reported by Ayers do not support this assumption.

In considering the etiology, heredity should be given an important place. Many instances are recorded in which glioma has manifested itself in the parents and children or in several children of the same parents. The opinion is general that should there be no recurrence three years after enucleation the prognosis is favorable, provided enucleation has been done before the disease has invaded the optic nerve or has ruptured the sclera.

Dr. Turner, in discussing glioma of the retina, emphasized the fact that a positive diagnosis is often difficult to make, and it is better to enucleate early when there is a mass causing a smooth, not wavy, detachment of the retina and loss of sight. The responsibility involves loss of life, and of the two evils we should choose the lesser.

Bilateral Spontaneous Cataract Formation in a Child Nine Years of Age

Dr. Frederick Krauss presented a case of bilateral spontaneous cataract formation occurring in a child nine years of age.

The cataractous lenses had a mother-of-pearl reflex and showed the physiological sectors very clearly. The left eye had light perception in the temporal field only, while the right eye showed normal field. Tension in the left eye was below normal. The Wassermann, von Pirquet, and urinary tests were normal. Transillumination of the right eye was negative, but showed a deep, broad shadow throughout the ciliary region, especially marked below. The previous vision had been good. Dr. Krauss believed that a possible explanation of the blindness and low tension in one eye was that it was due to a chorioretinitis with subretinal

hemorrhage in the anterior section of the eyeball, casting the shadow which the transillumination presented. The condition, therefore, was probably one of pseudoglioma in a child with cataract formation.

Case I.—Retinal vessel extending forward in vitreous.

Retinal Vessel Extending Forward in Vitreous

Case I.—Dr. George S. Crampton exhibited a colored man, aged forty-eight years, from the Wills Hospital service of Dr. William Zentmayer. About one year ago he stopped work on account of vertigo, vertical diplopia, and ataxic gait; these symptoms becoming progressively worse, he was shortly afterward confined to bed for five months. On admission to the clinic the gait was still somewhat ataxic, and he complained of prickly

sensations in hands and feet. The vision of each eye was 6/20; the pupils were equal, moderate in size, and reacted sluggishly to bright light. The eyes were straight under cover and the bulbar excursions full. Vertical diplopia and vertigo were no longer complained of.

Case II.—Retinal vessel extending forward in vitreous.

Aside from slight tortuosity of the retinal vessels and beginning pallor of the disk the right eye appeared to be normal. This was true also of the left eye, except that it was the seat of a long, glistening, rather pale vessel which sprang from the centre of the disk, and passing forward almost to the posterior pole of the lens returned to a nearby point after twisting three times about itself like a whip-cord. Pressure on the eyeball caused the vessel

to swing to and fro with each pulsation. The vessel, of the presence of which the patient was quite unaware, was probably an artery.

Case II.—Dr. Crampton referred to a similar case which he showed before the Section in 1911. This was a man, aged twenty years, who quite unaware that there was anything the matter with his right eye, presented himself complaining of poor vision in the left (6/60), which proved to be due to a high error of refraction.

The right eye, which had a negligible refractive error and a vision of 6/6, proved to be the more interesting. On ophthalmoscopic examination with a strong plus lens a slightly pulsating loop of vessels was seen close to the posterior surface of the crystalline lens. The vessel, which was bright red, appeared to spring from the lower nasal vein in the centre of the disk; from there it passed forward in a close spiral of many turns.

The fundus was otherwise normal and the vitreous quite clear. The grapevine loop was free from superfluous connective tissue, and seemed patulous throughout.

APRIL 15

Acute Axial Optic Neuritis as an Early Symptom in Disseminated Sclerosis

Dr. Edward A. Shumway pointed out that retrobulbar or, more accurately, axial optic neuritis had been recognized for a long time as an early symptom of disseminated sclerosis, and had been known to appear as long as twelve years before the nervous symptoms of the disease; but it was so infrequent in this country that he reported the case to call attention to the necessity of considering it in the presence of retrobulbar neuritis of uncertain origin. The patient had presented the characteristic symptoms of acute axial neuritis, when first seen in 1907, namely, unilateral rapid reduction of vision to 2/45 in one eye, pallor of the temporal half of the optic nerve, and central scotoma for

colors. Empyema of the posterior ethmoidal cells was found, and after drainage of the empyema and treatment with mercury and iodides, vision had improved to 6/22, and had remained stationary at that level for eight years, the scotoma persisting, although smaller in size. The condition had been ascribed to the sinus disease, but after a year nervous symptoms had appeared: gradual weakening of the legs, attacks of toe-drop, which appeared and disappeared, awkwardness in the use of the hands, and disturbance of sensation in the right index finger. The disturbances in the legs had gradually increased; ataxia of both upper and lower extremities had developed; deep reflexes had become exaggerated; ankle-clonus and the Babinski reflex could be demonstrated. The gait was typically spastic-paretic; nystagmoid movements were present in looking to the right or left, but no true nystagmus. The pupils reacted sluggishly to light. He had been examined exhaustively by Drs. Mills, Spiller, McConnell, and Price, and a diagnosis of atypical disseminated sclerosis had been made. Dr. Shumway thought the optic nerve involvement was to be considered as the initial symptom of the multiple sclerosis, rather than as the result of the sinusitis. He called attention to the exact similarity between acute axial optic neuritis and the condition in disseminated sclerosis, and quoted Wilbrand-Saenger's conclusions that the latter diagnosis was to be made only *when toxic, acute or chronic infectious processes attacking the optic nerve could be excluded.* If the visual disturbance showed a fleeting character, made no further advance, and improved spontaneously, or if a single nervous symptom appeared which could be considered part of disseminated sclerosis the diagnosis was more probable. Changeableness of the visual field defects, such as the addition of homonymous hemianopsia or irregular contractions of the peripheral fields, and striking variations in the severity of the visual disturbances were further indication of the central nervous disease.

Dr. George E. Price said that he had made the diagnosis of insular sclerosis in Dr. Shumway's case by the multiplicity of the symptoms and the exclusion of other conditions.

While Oppenheim states that multiple sclerosis is the most common of all the organic diseases of the central nervous system, it is certainly a comparatively rare disease in this country. Dr. Price had seen but few cases in his service at the Philadelphia General and Jefferson Hospitals.

Interesting features regarding the optic atrophy in multiple sclerosis were its frequent and early appearance, and the fact that considerable atrophy was apt to be attended by comparatively slight visual failure, owing to the tendency of the sclerotic process to involve the myeline sheath and spare the axis-cylinder.

Dr. Langdon stated that at the last meeting of the Ophthalmological Society of the United Kingdom, Paton reported three cases of transient papilledema in multiple sclerosis, lasting about ten days or two weeks. In the discussion he said he thought the condition was not noted more frequently because the cases were not studied at close enough intervals, the condition being so fleeting. He thought the condition was due to a patch of sclerosis in the nerve trunk blocking the retrobulbar lymphatic circulation.

Discussing Dr. Shumway's paper, Dr. de Schweinitz commented on its value, and emphasized the fact that it should never be forgotten that axial neuritis may indicate the future onset of disseminated sclerosis, and that this disease may develop from one to seven years after apparent recovery from the optic nerve inflammation. Dr. de Schweinitz emphasized the importance of most careful examination in all cases of unexplained amblyopia, and briefly detailed the case history of a patient observed by Dr. Carl Williams and himself, who for a time was regarded as a neurasthenic or hysterical person. The visual fields were characteristic of those of retinal tire, and the patient's general manner and ordinary symptoms strongly suggestive of hysteria, when a more searching examination, carried on under the direction of Dr. Spiller, revealed the fact that in all probability the patient was the subject of chronic lead poisoning, as she had been much exposed to the influence of this metal. Moreover, gradually the optic nerves, which in the earier periods of her discomforts had indicated no pathological change, assumed a pallor which was

confined largely to the papillomacular area. The patient is still under observation.

Dr. Shumway, in conclusion, said that optic neuritis and occasionally choked disk had been reported in disseminated sclerosis, and Uhthoff thought they were really more common than reports would indicate, but the atrophy of the temporal halves of the nerves was the most frequent appearance. He referred to the occasional complication with hysteria, and cited a case following traumatism to the head, which simulated disseminated sclerosis, even to the appearance of nystagmus and tremor, which because of the exaggeration of the symptoms had been diagnosed as either hysteria or malingering, and said the patient was reported to have recovered completely after the accident insurance companies had settled. Another point of interest was the etiology of multiple sclerosis; its pathology was disputed, but most writers were inclined to consider the lesions as due to an inflammatory process, which began around the bloodvessels in various parts of the brain and cord. The disease had been reported after various infectious diseases and intoxications, and he desired to suggest as a possibility in his case the absorption of toxins from the sinus empyema. Such foci of infection in the sinuses, teeth, and tonsils were looked for in iridocyclitis and uveitis, and while the theory had not been considered likely by the neurologists to whom he had talked, he nevertheless thought it worthy of consideration.

Sarcoma of the Choroid

Dr. William Zentmayer showed the patient from whom this specimen was obtained before the Section at the February, 1910, meeting. The card diagnosis was intra-ocular neoplasm, but the opinion expressed by the writer at that time was that because of the slow progress of the growth, the rounded contour, absence of signs of inflammation, and the age of the patient it was a case of sarcoma of the choroid, and the removal of the eyeball was advised. In the discussion Dr. Risley expressed his approval of this counsel.

The case was first seen by Dr. Zentmayer November 24, 1909, when the following notes were made: J. M., aged forty-nine years; freight train conductor (from the age of thirteen to twenty he followed the sea). There was nothing in the family or previous personal history relating to his present trouble. For the past thirty-five years he has not had a day's illness. His ancestry showed many instances of remarkable longevity. Two years ago he noticed a black spot in the nasal field of the left eye, and this has very slowly increased in size. One year ago he was examined for glasses by an oculist, but there was no intimation that there was anything seriously wrong with the eye.

The examination showed pupils of equal size; tension normal; anterior chambers of equal depth; conjunctiva injected. R. E., 6/6; L. E., 5/60. Form field showed slight contraction. There was an absolute scotoma up and in from fixation, quadrate in shape and about 17 degrees in its longest diameter, extending to within 8 degrees of fixation and 3 degrees of the horizontal meridian.

Ophthalmological: In R. E., no gross changes. L. E., media clear. Occupying the fundus midway between the papilla and the macula there was a mound-like swelling over which the retina appeared steel gray and somewhat mottled with a few glistening areas. The surface was rather smooth and the margins of the mass well defined, with the characteristic dark line around its base. The summit measured +6 D., the general fundus level being 1 D. There was no secondary detachment.

The physical examination made by Dr. Klaer showed nothing abnormal except a cystic goitre that had existed for a long time.

The patient refused to have the eye enucleated. Iodide of potassium was prescribed in increasing dose up to 30 drops t. i. d. He remained under observation just one year. During that period there was some fluctuation in the size of the scotoma, but at the time it was last charted it was smaller than at the first visit, but larger than the minimum size while under observation.

The elevation of the mass increased to 7 D., and it had extended

to the temporal margin of the papilla. Perhaps tired of the constant dinging to have the eye removed, he discontinued his visits and was not again seen until he came to Wills Hospital, April 24, 1914, seven years after the initial symptom, with acute secondary glaucoma. The eye had remained quiet except for a congestive attack during a spell of la grippe; the blind area spread so as to involve first the entire nasal field, then the temporal, until complete blindness ensued about one year ago.

The eyeball was congested, the cornea clear, anterior chamber shallow, pupil 3 mm., oval, axis 180 degrees, immobile. Lens cataractous, T. +2. No reflex from the fundus. He was admitted to the hospital and enucleation performed the following day. Dr. Brinkerhoff, the pathologist to Wills Hospital, has made the following pathological study:

Case.—J. M. C. The external appearance of the globe was normal. The cornea was clear. On making a horizontal meridian section the anterior chamber was shallow and empty. The lens was amber-colored and cataractous. There was no apparent change in the iris and ciliary bodies. The retina was attached only at the oraserrata and to the anterior surface of the growth. The subretinal space was filled with a clear jelly-like material. At a point near the temporal side of the optic nerve, and extending to about the location of the fovea centralis, there was a mushroom-shaped, pigmented mass, measuring 10 x 7.5 mm., extending into the vitreous chamber. The optic nerve was deeply cupped, probably glaucomatous, due to the increase in the intra-ocular tension caused by the neoplasm.

Microscopically the growth was a mixed-cell melanosarcoma; the spindle cells vastly predominate. The cornea was normal. The anterior chamber was shallow and empty. The canal of Schlemm was absent on both sides. The iris and ciliary bodies were atrophic. The retina was degenerated, very little remaining except some of its nuclear elements. The lower portion of the retina was in close contact with the growth. The choroid was atrophic and contained numerous hemorrhages. The growth penetrated the elastic lamina and formed a mushroom-shaped

nodule in the posterior part of the vitreous chamber. Scattered through the growth were many hemorrhages. The chromatophores were increased in number. The optic nerve was not involved.

Dr. Zentmayer, in closing, said he simply wished to call attention to the long duration of the first stage. The patient had noted a scotoma for two years before he came under his observation, and four and a half years elapsed after that before secondary glaucoma set in. When first observed with the ophthalmoscope the growth must have been about 1.5 mm. in diameter, as it did not occupy more than half the area between the papilla and macula.

Concerning Certain Postoperative and Post-traumatic Complications and their Treatment

Dr. G. E. de Schweinitz, among other complications, described a case of filamentous keratitis appearing shortly after a cataract extraction, of unusual elaboration, and emphasized the value of holocain in dissipating the lesions. He discussed the occasional value of large doses of quinin in the treatment of uveal tract inflammations of traumatic origin, and referred to the belief that quinin in acute inflammations might arrest inflammatory exudation and allow extruded cells to wander from diseased areas, or that it might increase the phagocytic power of the blood. He also discussed the theory that it might have an influence on showers of leukocytes developing periodically, somewhat analogous to the influence of the drug on malarial parasites. Clinically he was satisfied that occasionally the drug was of distinct service in these circumstances.

He also described some cases of recurring hyphema after cataract extraction, when there had been no complication during the operation and no condition in the patient which ought to give rise to this state of affairs. All of the eyes thus affected ultimately recovered, and he attributed some value to the administration of calcium lactate. He also discussed the value of thyroid extract in these circumstances, as well as that of coagulose and pituitrin. Dr. de Schweinitz thought that, if opportunity

arose, optochin therapy should be tried in localized postoperative and suppurative infections if they were of pneumococcic origin, and referred to a case of infection following traumatism which had occurred in the practice of a colleague, where apparently the process had been favorably modified by the use of ethyl-hydrocuprein.

Discussing some of the remedial agents which have been employed to combat various types of iridocyclitis which follow traumatism, particularly in the ciliary region, Dr. de Schweinitz spoke favorably of what is ordinarily known as Schirmer's mercury treatment, although he himself had been unaccustomed to use the inunctions, and had depended upon calomel given continuously for a number of days. He thought, as Axenfeld had said, when referring to the relationship of pyogenic organisms to various types of relapsing subacute and chronic iritis, that the value of the mercurial treatment to modify a definite organismal wound infection could not be decided by the findings in the human eye. If it be true that the increase of hemic fibrin is one of the characteristics of inflammation, it would be possible, he said, quoting the words of a well-known therapeutist, that there was more or less antagonism between the processes of mercurialization and of inflammation. Whatever the explanation of the value of this drug in these circumstances is, the clinical fact remained that its service was a great one. He thought that not infrequently a combination of mercury and the salicylates was of value in combatting various types of traumatic uveitis. In these circumstances he was accustomed to use the mercury after the manner of Schirmer by inunctions, and salicylates or aspirin by the mouth.

Dr. Holloway stated that he thought Dr. de Schweinitz probably referred to a patient who had recently returned to the University Hospital about two years after cataract extraction. During Dr. de Schweinitz's absence from the city an uncomplicated cataract extraction had been performed on the right eye, and on the fourth day an iridocyclitis developed. After subsidence of the inflammation there was a slight drawing up of the iris with

occlusion of the coloboma. A Zeigler operation was performed, and with correction 6/6 vision was obtained. The patient was not seen again until several days ago when he returned stating that the vision in the other eye, also cataractous, was failing. Upon examination it was found that the vision of the right eye was 6/22, tension +1; pulsation of the retinal vessels and a beginning cup in the nerve head. Examination with a loupe showed that over the upper and inner sector the base of the iris was glued against the posterior surface of the cornea. In reference to the use of ethylhydrocuprein, Dr. Holloway stated that the patient to whom Dr. de Schweinitz had referred presented a deep corneal infiltrate with superficial ulceration and marked iridocyclitis with hypopyon, presenting an appearance strongly suggesting ulcus serpens. Several bacteriologic examinations failed to show any organism more virulent than the staphylococcus albus. Vaccines were used and 500,000,000 injected on six different occasions, apparently without any affect. Decided improvement began immediately after the use of ethylhydrocuprein hydrochloride 1 per cent. watery solution. Dr. Holloway stated that he was uncertain in this case whether the improvement was dependent upon the use of the drug or whether its use happened to coincide with the turn for the better. Despite the bacteriologic examinations he was inclined to believe that the corneal lesion in this case was dependent either upon the pneumococcus or the Morax-Axenfeld bacillus. He had seen good results from ethylhydrocuprein in several cases of pneumococcus conjunctivitis.

Dr. Shumway reported improvement in a case of endogenous infection, after preliminary iridectomy, from pyorrhea alveolaris, by the use of injections of emetin hydrochloride. After the eye had quieted, the cataractous lens had been extracted, and vision of 6/22 secured by iridotomy with de Wecker's scissors.

Dr. Zentmayer stated that he had used ethylhydrocuprein in five cases of pneumococcus ulcer of the cornea and had been disappointed in the results. In none of the cases was the infection virulent, yet in one there was complete perforation and in another the destruction reached Descemet's membrane. The chemical

was used in 2 per cent. solution applied to the ulcer once daily, and in 1 per cent. dropped into the conjunctival sac every three hours.

The value of holocain in herpetic and filamentous keratitis as pointed out by Dr. de Schweinitz is undoubted. In a recent case seen at Wills Hospital forty-eight hours after holocain had been added to the previous treatment the condition had entirely subsided.

Alcoholic Injection in the Facial Nerve for Facial Spasm

Dr. George M. Dorrance described two distinct types of contortion of the facial muscles—one being facial spasm, a good picture of which may be obtained by faradization of the facial nerve, and the other tic convulsif, which is always the replica of a perfectly natural and physiological movement.

Etiology. In the etiology the most frequent cause is the irritation of the fifth cranial nerve, especially in the region of the eye.

Anatomy. Facial spasm has no known morbid anatomy.

Diagnosis. Facial spasm may be a spasm of all the muscles supplied by the seventh nerve, or it may be of one or more muscles, such as in blepharospasm where only the orbicularis palpebrarum and associated muscles are involved.

Treatment. In the literature one notes that treatment of this condition has been rather unsatisfactory, many drugs, etc., having been employed. In this method we attempt to paralyze the nerve, and in this way prevent the muscle from contracting for some time, in the hopes that the muscle will by this rest overcome its tendency for spasm.

Technic. The alcoholic injection consists in injecting the nerve as it leaves the stylomastoid foramen, which is easily done by passing the needle upward and slightly forward from the tip of the mastoid, the depth being 1.5 cm. The other consists in injecting the branches of the seventh nerve as it leaves the parotid gland. In this way, one is able to inject the nerves as they go

to certain groups of muscles; for instance, for blepharospasm, inject over the zygoma posterior to a mid point between the external angular process of the frontal and external auditory meatus. In that injection 1 to 2 c.c. If it is desired to paralyze the muscles that elevate the upper lip, introduce the needle on the same level one-half inch below the zygoma and introduce 1 to 2 cm.

Conclusions. If the injection is successful the muscles are paralyzed; the motor paralysis is greatly overcome; in from six to eight weeks free motion will have returned, but the spasm usually does not return.

Prognosis. The spasm frequently recurs in several weeks. It may not recur for months and frequently it never recurs.

Dr. Holloway stated he felt the Section was much indebted to Dr. Dorrance for bringing this subject to the attention of the members. Only recently he had had a patient with excessive blepharospasm, at times producing practically complete closure of the lid, which he finally determined to be of hysterical origin. The condition was so marked that when the patient first came under observation he had spoken to a neurologist as to the advisability of alcoholic injections and had been advised against the use of this treatment in connection with a motor nerve. Since that time the condition had practically disappeared under the use of electricity. He was very glad to hear that Dr. Dorrance had had such satisfactory results after this procedure. Dr. Dorrance's method is in line with the procedure of Van Lint who has resorted to temporary paralysis of the facial nerve in cataract cases complicated with blepharospasm. He uses injections of novocain and adrenalin along the lower and outer margin of the orbit, in order to catch the terminal branches of the seventh. It also recalls to mind the procedure adopted by Vail in cases of delayed closure of the wound after cataract extraction. Inasmuch as he believes that this is frequently caused by an involuntary spastic contraction of the orbicularis palpebrarum he severs the orbicularis attachment of the external canthus by an incision directly upward and downward made with blunt scissors.

In reply to Dr. Ring, Dr. Holloway stated he really did not know what current had been used, as it had only been employed with the idea of conveying suggestion. The patient had been sent to a neurologist for treatment. After the first application the patient had complained so bitterly that no current at all had been used for two or three visits.

Discussing Dr. Dorrance's paper, Dr. de Schweinitz referred to some cases of blepharospasm which had yielded, temporarily at least, to alcohol injections given in the ordinary way, not as Dr. Dorrance had described. While fully agreeing with the essayist that in most instances drugs were useless, he had occasionally observed a distinct amelioration when very large doses of gelsemium had been administered.

OCTOBER 21

A Case of Congenital Paralysis of the Externus with Retraction of the Globe in Adduction

Dr. William Zentmayer exhibited a girl, aged eleven years, who had been sent from school because of defective vision. She had frequent severe headache and slight asthenopic symptoms. On the left side there was slight enophthalmos, complete paralysis of the external rectus muscle, and narrow palpebral fissure. In looking to the right there was a little restriction of the inward rotation of the globe, accompanied by a marked narrowing of the palpebral fissure and some retraction of the globe. The upward rotations were not affected. In the right eye there was a strand of retained pupillary membrane. Both eyes were H. 3 D.

There is anatomical proof that in some of these cases the phenomena are due to the existence of a fibrous cord in place of a normal rectus muscle.

Buphthalmos Complicated by Measles and History of Tuberculosis

Dr. S. Lewis Ziegler exhibited a girl, aged twelve years, who applied to the Wills Hospital for treatment three months previously, at which time the vision of R. E. was 8/200. There was marginal blepharitis and interstitial infiltration of the cornea with central macula (2 mm.) and some vascularity. The anterior chamber was somewhat deepened and the iris normal and responsive to light. No fundus details could be seen. Tension = 6 mm. Hg.

The L. E. had light perception and projection, large buphthalmic cornea with central macula (2 mm.), and some vascularity and marked interstitial infiltration. The anterior chamber was deep and the iris normal in color, 13 mm. wide, with sluggish pupil. No fundus details were visible. There was slight scleral injection and ciliary stretching. Tension = 43 mm. Hg. Blepharophimosis, slight roughness of conjunctiva. Lacrimal obstruction. Urine negative.

Her family physician stated that the condition had existed for some years and thought it followed an "attack of measles complicated with a tuberculous element." Father died of tuberculosis. Patient had enlarged cervical glands. Had measles nine years ago. Was treated by various oculists and at a New York hospital; condition not improved.

Admitted to hospital six weeks ago. Operation under ether; external canthotomy and rapid dilatation of tear ducts. Von Pirquet positive. Tuberculin $\frac{1}{500}$ mg., ten injections. Phylacogen 2 c.c., ten injections. House tonic. Eserine gr. j in both eyes. Ocular condition and general health greatly improved. Both cornea have become clearer and the left globe perceptibly smaller. Slight reduction in size of cornea and depth of anterior chamber. Iris now 12 mm. wide. Discharged one week ago. Corrected vision R. E., S +2.25; D. = 20/70. L. E., S. −0.75; D ⊂ C −1.25; D. Ax. 30 = 20/200.

Dr. Holloway stated that at the Overbrook School for the Blind there were a number of cases of buphthalmos that had passed through various stages of the disease, and in at least one case it had been necessary to enucleate first one eye and then the other. In two instances he had seen the one eye become smaller with lowered tension, and had rather attributed this change in advanced cases to degenerative processes.

Spontaneous Rupture of a Glaucomatous Eye-ball

BY G. E. DE SCHWEINITZ, M.D., AND H. W. HOW, M.D.

The patient, a woman, aged about sixty-five years, reported two months after an attack of acute glaucoma in an eye containing a cataract, from which eye, however, the cataract had not been extracted. The affected eye had a tension of +3, an abolished anterior chamber, the lens being wedged into the pupil space and the cornea exceedingly hazy. Light perception was abolished. Enucleation was advised but declined. About one month later, preceded by sudden intense pain, blood streamed suddenly from the lower and inner margin of the cornea. The eye was enucleated. The different varieties of spontaneous rupture of the eye-ball were discussed, namely, those which occur when the cornea has been ulcerated and those which occur without such ulceration, and a brief review of the literature was made. Those ruptures which occur in association with sarcoma of the choroid were also discussed. Microscopic examination revealed a complete rupture of the corneal fibers 2 mm. from the limbus, with prolapse of the margin of the iris into and between the lips of the wound. The cornea showed deep keratitis and infiltration, but no ulceration; iris, ciliary body and choroid thickly infiltrated with blood corpuscles. The origin of the hemorrhage was undoubtedly from the choroid.

Dr. Turner referred to a case which had been seen by Dr. de Schweinitz in consultation. An iridectomy had been done for the relief of glaucoma with apparently normal healing of the wound.

Ten weeks later the lens was seen to protrude and was removed with forceps. On examination the eye was found to be the seat of a sarcoma of the choroid. There has been no evidence of sarcoma of the orbit after five years.

Dr. Sweet referred to a case which he had previously reported of the spontaneous rupture of a blind glaucomatous eye-ball in a man, aged seventy-five years. There was no apparent ulcer of the cornea at the point of rupture. Under treatment the corneal wound healed, but the eye-ball became slightly atrophic. The man would not consent to enucleation. He was seen by Dr. Sweet several years later, and the eye was quiet, so it is probable that there was no intra-ocular growth.

Leucosarcoma of the Choroid

Dr. de Schweinitz and Dr. How briefly recorded the history of a male patient, aged forty-one years, whose left eye had presented on examination a large retinal detachment, the height of which was +6 D., situated below and to the nasal side. Transillumination had been completely interrupted, the vitreous was filled with numerous fine opacities, and there was somewhat of a flush on the scleral expanse which was directly over the growth. Section of the enucleated eye-ball showed in its posterior third a grayish-white, lenticular-shaped mass 6 mm. in width and 11 mm. in length. The point of origin appeared to be from the choroid about 1 mm. from the edge of the disk, and the external surface of the tumor was in close contact with the sclera. The tumor was composed of small cell tissue of the embryonic connective-tissue type, each cell possessing a relatively large nucleus, surrounded by a small amount of cytoplasm. The origin of the tumor was from the vascular layer of the choroid, including the choriocapillaris. There was no pigment in the growth. In presenting this growth some reference was made to the various varieties in which the endotheliomas and sarcomas present themselves in the choroidal tissue, and a brief reference to the use of radium in the treatment of sarcoma of the choroid was made, but the authors were unable

in their own experience to record any satisfactory result from this agent in these circumstances.

Dr. Shumway said that he had seen the patient with sarcoma of the choroid, which was being treated at the Oncologic Hospital by radium, but knew nothing of the results, as he had seen her only once.

Expulsive Spontaneous Hemorrhage Two Days after Cataract Extraction

BY G. E. DE SCHWEINITZ, M.D., AND H. W. HOW, M.D.

Two days after a perfectly normal extraction of cataract (combined extraction), suddenly preceded by sharp pain, nausea, and vomiting, an expulsive hemorrhage took place, the intensity of the hemorrhage being such that it was deemed advisable to make an immediate enucleation. Microscopic examination revealed that the lips of the corneal wound were covered with conjunctival epithelium over the entire thickness of the cornea. There was a slight marginal edema, with polynuclear and mononuclear infiltration. The iris and ciliary body were engorged with blood, and the hemorrhage which filled the globe was made up entirely of red blood cells. Apparently the hemorrhage took its origin from the vascular layer of the choroid, and the clots had a somewhat laminated structure.

Dr. S. D. Risley was greatly interested in Dr. de Schweinitz's paper, particularly in the case of hemorrhage occurring on the sixth day after the extraction of cataract. He thought that on approximately the fifth day after both extractions and iridectomies, hemorrhages into the anterior chamber were not infrequent, but did not recall any case in his own experience where the wound had opened and permitted the blood to escape from the anterior chamber, as in the case reported by the essayist. Except in the case of direct injury, he thought the prognosis was usually good. In his early experience he had ascribed the hemorrhage to injury of the eye by the patient during sleep, or to straining in the act

of urination, but was now convinced that they were often spontaneous and occurred through the lack of support by a suitable bandage, and by the movements of the patient during the first days out of bed. He had often seen a gaping of the lips of the section, or a bulging of the wound, which had before been smooth, a day or two days after removing the dressings and allowing the patient to sit up, the bulging disappearing after reapplication of the bandage. It was conceivable that this distending process might in certain cases lead to a reopening of the ciliary zone of bloodvessels in the iris which had been cut across by the section, either in the extraction of the cataract or in iridectomy for increased tension. The lesson taught by these cases he thought was not to remove the dressings too soon and to warn against too great freedom of action at this critical time of their convalescence.

Dr. Shumway, referring to Dr. de Schweinitz's case of hemorrhage after cataract extraction, said that in a case which he had had at the Philadelphia General Hospital, during the past summer, in which the hemorrhage occurred at the time of operation, the bleeding from the interior of the eye was so profuse and persistent that it was necessary to resort to injections of horse serum. The difficulty in checking the hemorrhage from the choroidal vessels which occurred after opening of the globe was presumably due to the absence of muscular fibers in the walls of the veins, and he thought that horse's blood serum might prove of value in small recurring hemorrhages, such as had been mentioned by Drs. de Schweinitz and Risley.

Dr. Hansell stated that his experience included many cases of hemorrhage into the anterior chamber, both spontaneous and traumatic, after cataract extraction. One case was that of a man in whom a profuse hemorrhage, filling the anterior chamber and forcing open the wound, occurred on the fifth day after operation, while he was seated quietly in a comfortable chair. The operation had been smooth, the healing rapid, with no complication whatever, and he had been promised that he could return to his home in two more days. Like most cases, this one regained full acuity of vision. Dr. Hansell agreed with the gentleman who

said that the prognosis of hemorrhages of this character is favorable; it being equally good after traumatism unless the hemorrhage be complicated with injury to the coats of the eye.

Avulsion of the Lids with Bilateral Sixth Nerve Palsy

Dr. T. B. Holloway before presenting the case stated that he exhibited the patient inasmuch as she illustrated very well the favorable result that can be obtained in some cases of emergency plastic surgery. This patient, while walking on the pavement, was struck by an automobile and pinned against a wall. She was taken to the Polyclinic Hospital and admitted to the service of Dr. Jopson and his associate, Dr. Speese. Through the courtesy of the former the patient was seen some half-hour later, when she was on the table ready for operation. She was unconscious, and the following injuries were noted: There was a wound that began in the left frontoparietal region about five inches above the centre of the eyebrow, extended obliquely forward through the middle of the eyebrow, curved inward along the upper border of the inner half of the upper lid, curved around the internal canthus, and extended downward along the side of the nose to a point external to the corner of the mouth. This flap could be reflected outward, exposing the skeletal and muscular structures lying anterior to a line connecting the beginning and ending of the wound. In addition to this there was a wound that began just below the internal canthus, and extended outward below the lower margin of the orbit to a point beneath the external canthus. The skin of the upper lid was completely detached from the upper tarsus, and the upper tarsus with the underlying conjunctiva was completely torn away except at its outer extremity, where it remained attached by the external canthus to the outer fourth of the lower tarsal cartilage, which was also torn loose. The skin of the lower lid was included in the narrow tongue-like flap lying between the horizontal incision above referred to and the margin of the lid. This in turn was detached from its tarsus, and this structure was split into three pieces, an outer fourth, which was torn loose, a middle two-fourths

remained *in situ*, and the inner fourth, which was missing. In addition to this there was a lacerated wound of the posterior part of the scalp, and bleeding from the ear and nose.

Dr. Speese inserted sutures in the upper and lower extremity of the wound in such a way as to crowd the flaps toward the internal canthus. Dr. Holloway then inserted several buried catgut sutures in the fascia and muscles of the brow. Buried catgut sutures reunited the tarsus to the conjunctiva at the fornix. While it was impossible to reattach the levator, an attempt was made to connect the lid with the fascia and muscles above in order to secure some action from the frontalis muscle. Sutures were inserted uniting the split lower tarsus, and the skin was then united to the lids by a row of sutures along the palpebral margin. The greatest trouble was in finding suitable anchorage for the two lids at the internal canthus. All the wounds healed by primary intention, but owing to cicatricial contraction there was some drawing outward of the internal canthus with displacement of the palpebral fissure. There was also marked ptosis of the upper lid.

Owing to the existence of a bilateral external rectus palsy, Dr. Holloway felt that it was not advisible to attempt any operation for the relief of the ptosis. The unique feature of this case was the fact that while both lids were torn away there was not the slightest abrasion of the cornea or other demonstrable lesion of the globe. Owing to the extent of the injury there was also a partial peripheral seventh nerve palsy.

Perforating Wound of Cornea from Blank Cartridge

Dr. G. S. Crampton exhibited a woman, aged thirty-five years, who two and one-half months previously was shot in the face by a blank cartridge fired from a revolver held about two feet distant.

The face was badly powder-burned from midforehead to tip of nose, with involvement of both eyes, the left being mostly affected.

On examination immediately after the accident it was seen that the eyes had been slightly closed at the time but not sufficiently

to prevent severe powder burns of both corneas. The left cornea was perforated in several places, as could be seen by the deposits of carbon on the iris and the presence of air bubbles and a small amount of blood in the anterior chamber, together with small ragged wounds of the cornea.

Apparently but little aqueous was lost. A triangle of exposed conjunctiva at the nasal side of the left cornea was so badly burned that it was necessary to excise and replace it by a flap of unburned conjunctiva which was drawn over and sutured.

About two hours were spent in a patient endeavor to remove the powder grains from the cornea, conjunctiva, and skin by rubbing with cotton applicators and peroxide of hydrogen. Many of the black granules being forced to the surface of the skin by the action of the peroxide on the blood in the wounds. Cocain was freely used to prevent pain. Afterward atropin and liquid albolin were instilled and dressings applied.

The reaction was not as severe as expected and aside from a slight iritis of the left eye and a 1 mm. hypopyon which made its appearance on the eighth day there were no evidences of infection.

Dionin in saturate solution and holocain were used with the atropin and a gradual recovery resulted. Thirteen days after the injury the vision was R. E. = 6/10; L. E. = 5/35 illit. Today it is R. E. = 6/6; L. E. = 6/9.

The powder marks on the skin are gradually being cut out by encircling them with the sharp point of a knife and excision of the tiny piece of skin with scissors.

NOVEMBER 18

Perforating Wound of Cornea, Iris, and Lens

Dr. G. Oram Ring exhibited a patient showing the end-result in a perforating wound of cornea, iris, and lens, in which operation based upon negative *x*-ray findings resulted in an absolutely

quiet eye with approximately normal vision where enucleation had previously been advised.

Nine months before Dr. Ring was consulted, the patient, a male, aged thirty-two years, while turning steel mandrels on a lathe was struck in the right eye.

The inflammatory symptoms lasted two weeks. The vision gradually grew dim and upon the date of examination only light perception and projection were present. There was a zone of pericorneal flush down and in which increased under examination, with moderate lacrimation.

A small corneal scar down and in from the pole was present, and in the iris could be detected a minute slit-like perforation in a position corresponding to the corneal perforation.

The lens was almost completely opaque, the iris reacted normally to light, and no adhesions were present; dilatation under mydriatic was moderate.

The vision of L. E. was 6/5. No gross changes in the fundus were present but disk margins up, in, and down were obscured. No lacrimation or photophobia. Two *x*-ray pictures by Dr. William Sweet were negative, notwithstanding the clinical picture presented.

Operation consisted of a vertical incision from the lower to the upper dilated pupillary border into the lens with a Hays-Ziegler knife, followed by a second two weeks later.

Swelling and absorption were entirely uneventful and painless, and a final V-shaped capsulotomy four months later made possible a vision approximately normal with an entirely mobile pupil.

During the period in which the above case was under observation, two other cases of penetrating foreign body, each with traumatic cataract, were under treatment. The one was an approximately central perforation of the lens with negative *x*-rays, absorption was uneventful, pupil mobile, no adhesions, with a final discission yet to be done.

The second was a perforation through cornea, iris and lens, down and out just within corneal limbus, with infected ulcer. *X*-rays showed the foreign body in the lens.

When all active symptoms had subsided, extraction of soft lens was uneventful, with extrusion of foreign body in lens substance.

Recovery was uneventful, with faint posterior capsule still to be incised.

Dr. Ring's conclusion was that while an *x*-ray will not in every case locate a foreign body, if the latter is exceedingly small with sharp side toward plate, but the failures are so very rare in the presence of a skilled technic that one is warranted in basing an operative judgment upon its findings.

Obstruction of Retinal Circulation (Thrombosis) in Cardiorenal Disease

Dr. G. Oram Ring exhibited a case showing sudden retinal obstruction (thrombosis) in a case of cardiorenal disease.

The patient, a male, aged fifty-seven years, acknowledged to excessive use of tobacco and alcohol. About two years ago a brief attack of hemiplegia lasted three days. On recent examination the arm and leg were spastic on left side, knee-jerk was much increased; ankle-clonus and Babinski present on left side, with hemiplegic gait and arm held in characteristic position.

Wassermann negative; albumin and granular casts were present in urine. Heart enlarged to left. Mitral systolic murmur. Accentuated aortic second sound.

Blood-pressure on admission, 250 and 130; two weeks later, 200 and 120.

One year after cerebral attack vision in L. E. suddenly become foggy but returned the following morning. Three months later there was a temporary, almost complete loss of vision in R. E. with restoration the following morning, but four days later awoke to blindness in this eye. Neither light perception nor projection.

Pupil semidilated and immobile to direct light, but maintained a consensual reaction.

The condition of R. E. was more interesting for purposes of study, and primarily presented the picture of so-called embolism of central artery.

The macular region showed red through the whitish haze, superior and inferior arteries being seen as white cords. The nerve was covered with dilated cilioretinal vessels. With the falling of the blood-pressure these same arteries showed as a series of broken red lines, and some days later were manifest as a continuous red line, contracted but filled.

Hemorrhages and lipoid infiltration with cholesterine deposits were evident in macular region.

The views of Rokitansky, Virchow, Thoma, Jores, and Koster were given, special emphasis being laid upon Koster's insistence that there is almost always a demonstrable continuity between the patches of endarteritis, mesarteritis, and periarteritis.

The vasomotor crisis of Pal with sudden constriction and dilatation of the arteries in association with the organic changes in the vessel walls furnished a likely explanation for the interesting and comparatively prompt reëstablishment of the blood current in vessels that a few hours previously had the appearance of white cords.

Reference was made to the extreme rarity of true embolism, the process being regarded as thrombotic in arteries the subject of degenerative changes, especially a progressive proliferation of the intima with consequent contraction and restoration made possible by a retrogression of the process.

Reference was made to Harms's conclusions that a diagnosis of true embolism is permissible only when we have excluded disease of the vessel walls, when a defect of the valves of the heart or some other plausible condition of disease can be demonstrated, and when signs indicative of a thrombotic occlusion of the artery are not present.

Dr. Zentmayer: The condition which Dr. Ring has described in his paper as an "edema of the retina" has always been, to me, an interesting phenomenon. In 1901 I reported a case of embolism of a cilioretinal artery and called attention to the limitation of the opacity to the area of distribution of the vessel, and expressed the view that the generally held opinion that this was due to an edema of the retina, seemed untenable in view of the above fact,

and the further facts that in branch embolism there is the same festooning of the opacity about the terminals of the twigs of the artery and that in obstruction of the central artery, in the presence of a cilioretinal vessel, the area supplied by this vessel remains transparent, notwithstanding that the surrounding retina is opaque. If the opacity were due to an edema, it would include this area just as it does in obstruction to the main trunk of the central artery. Furthermore, edema is not a marked symptom of obstruction to an artery, but is rather an accompaniment of venous obstruction. Frost, while giving no reason for his opinion, states that the opacity is probably of the nature of a postmortem change. It is now more generally conceded that the opacity is due to a molecular necrosis.

Dr. Posey referred to a paper on "Transient Monocular Blindness," which he read before the Section some years before, in which he called attention to a number of cases presenting transient attacks of loss of sight, afterward culminating in thrombosis of the central artery of the retina. He said in several of these cases death had occurred about two years after the occurrence of the thrombosis. He referred to a case reported by Wagenmann in which there were all the ophthalmoscopic signs of embolism of the retina, but in which a later pathological study showed evidences of arterial sclerosis, but without clot formation, Wagenmann having attributed the blindness to spasm of the central artery of the retina.

Dr. Posey said it was interesting to note how long a period might elapse after blindness had ensued before vision was regained. As well as he could recall, in one of his cases the blindness had persisted for nearly twenty-four hours. In Dr. Ring's case the blindness had apparently persisted over a period of twelve hours. As a point in differential diagnosis between embolism and thrombosis of the central artery of the retina, Dr. Posey said that in the first condition blindness would ensue without premonition, whereas in thrombosis there were usually the attacks of transient loss of vision which had been under discussion.

Dr. Holloway stated that in the patient recently observed at the University Hospital, and to which Dr. de Schweinitz had referred,

there was present the usual picture of the subsiding manifestations of a thrombosis of the central artery of the retina. The field was taken on two different occasions by screening off the right eye and allowing it to fix, so that the image of a candle flame assumed the proper position on the cornea of the eye under examination. A light was then used for mapping the field, which in each instance tended to assume the shape of a vertical ellipse. When a beam of light was thrown into the eye with the ophthalmoscope the patient could quite accurately tell when the light impinged on the retina just off the temporal side of the disk, but the recognition was by no means as prompt to the nasal side. It was thus assumed that the peripapillary anastomosis was much better established about the temporal portion.

Dr. S. D. Risley congratulated Dr. Ring on the admirable results secured from his operative procedure. He regarded the case as one of great interest, however, not only from the point of view of operative technic in a doubtful case, owing to the possible presence of a foreign body in the vitreous chamber, but as illustrating the importance of attachment between the iris and the anterior capsule of the lens. There was some ciliary injection and tenderness of the ball which persisted until the discission of lens and capsule had removed the tension consequent upon this attachment of iris and capsule. Dr. Ring had given him the opportunity to study both the cases presented. In the second case, at the time he had seen it, the arteries were both apparently of normal size but obscured, as were all the other details of the fundus, by what he had regarded as an edema, a term which he still felt like using for want of a better word. The bright red spot at the macula had given place to a light chocolate-brown color, more or less quadrate in shape. At the time he had the opportunity to study it there could be no thought of a plug of the central artery of the retina, and he had regarded the case as one of blocking through arterial disease. He had always had difficulty in comprehending the exact state of the tissues in the fundus presenting the appearance he had for so long regarded as an edema. There was certainly some infiltration process present, since the appearance of the retina

differed so widely from that seen in a mere detachment by fluids behind the retina, and he recorded one instance of sudden blindness, which in the end proved to be tubercular in origin, in which the entire nasal half of the ophthalmoscopic field was a grayish-white elevation, and which he had regarded as an edema or infiltration of the retina and choroid. Near its centre could be seen with the electric ophthalmoscope a denser white spot, which under the administration of old tuberculin and rapid disappearance of the edema, left a large atrophic area in the choroid at the site of the tubercular deposit.

Mucocele of Frontal Sinus Simulating Tumor of Orbit

Dr. William M. Sweet exhibited a case showing the results of operation upon a mucocele of the frontal sinus that simulated a tumor of the orbit. The patient, a woman, aged forty-three years, had suffered for two years with severe frontal headache. Four months ago she came to the Wills Hospital with slight proptosis of the right eye, diplopia in upward rotation, and a small tumor at the inner portion of the orbit, somewhat firm in consistence, and not altered in size by pressure. Wassermann was negative, as were also examinations of the nasopharynx and of the sinuses by the Roentgen rays. Alteratives were given, but the orbital mass gradually increased in size, and the eye was pushed farther down and out. Later there was evidence of slight fluctuation in the tumor. Radiographs did not show any blocking of the frontal sinus, although there was necrosis of the floor. Again examination of the nasopharynx was negative. A modified Killian operation was decided upon, and was performed by Dr. F. O. Lewis. After the skin covering the frontal region was turned back, the bone was found to be discolored, and the finger broke through into the sinus. The floor of the sinus was gone and a large pocket of pus extended into the orbit. Both sinuses were one large cavity, with the superciliary ridge of the right side necrosed, and also the anterior ethmoid cells. All the diseased bone was removed, and drainage carried into the nose. Recovery was rapid, with only

moderate disfigurement. The case was unusual in that at no time were there any nasopharyngeal symptoms, and that expert radiographic examinations were negative.

Double Cataract Extraction in Diabetes Mellitus

Dr. Howard F. Hansell exhibited a colored man, aged twenty-seven years, who was admitted to the Jefferson Medical College Hospital on June 5, 1915, suffering from diabetes mellitus and double cataract. For five months the urine had not been free from sugar, the percentage varying from 6 per cent. to 10 per cent.; the greatest amount (August 18) was 435 grams, the least 118 grams. The quantity of urine averaged about two quarts.

Dr. Hansell stated that he brought the patient before the Section not to demonstrate a new operative procedure or unusual technic, but to show perfect recovery from cataract extraction in each eye, and a discission of after-cataract in the right eye, in a patient with diabetes of marked type.

The operations were uneventful, the wounds healed in twenty-four hours, no undue inflammation followed, and the result was good vision in each eye and ability to resume his work.

He had always felt that the prognosis of operation on patients in whom the amount of sugar exceeded 2 per cent. was unfavorable. In this patient there was little or nothing to lose, and the result fully justified the operation.

Dr. Zentmayer asked Dr. Hansell whether prior to the operation the patient had been on a restricted diet or on a strict antidiabetic diet. This he thought of interest in view of a recently expressed opinion, the basis of which he failed to comprehend, that there was great danger of tissue necrosis and death in coma if the sugar intake was greatly diminished before operating.

In answer to Dr. Zentmayer's question, Dr. Hansell stated that the patient had been under a strict antidiabetic diet and antidiabetic remedies for five months before operation, but that neither the percentage of sugar nor amount of urine passed seemed to be much modified.

Retinitis Circinata

Dr. Harold G. Goldberg reported a case of retinitis circinata in which the typical changes were observed. The patient's family history was interesting, and suggested the possibility of a congenital relationship. The man denied venereal infection, but exhibited a +2 spinal fluid Wassermann reaction. Both eyes were affected, the changes in each being very much the same. The characteristic appearance was a purplish-red area occupying the macular region, directly in the centre of which was a glistening yellow spot; encircling the macular region there was a zone of healthy retina surrounded by a ring of pale pink to bright white spots having an apparent size of from one and one-half to three mm. in diameter. The circle was irregular in outline, but was uninterrupted in its extent. The spots showed no traces of pigmentation either at their centres or at their borders. The remaining fundus was healthy. Under treatment the vision of R. E. improved from 2/22 to 5/150 and that of L. E. from 2/35 to 4/150.

A Few Clinical and Pathological Notes on Two Epibulbar Growths

BY G. E. DE SCHWEINITZ, M.D., AND H. W. HOW, M.D.

The first of these patients, a man in middle life, had a small growth at the lower corneoscleral junction, which prior to his coming under the care of the University Dispensary had been cauterized twice with trichloracetic acid, apparently with a good result, but eight months later it reappeared, and at this period of time he came to the University with a small fleshy mass at the corneal margin, down and slightly out, about 2 by 4 mm. and 1.5 mm. in height. A number of vessels ran to it from the lower area. There were no other lesions in this or the fellow eye. The small growth was dissected from its bed, healing was kind, and there was no reappearance until eight months later, when he returned with a typical recurrence. This was now submitted to radium

applications. These produced an exceedingly sharp reaction, at first a conjunctivitis, but later a mild iritis, and for a short period of time a slight hypopyon. This reaction yielded to suitable treatment and the eye has become quiet and the growth diminished to about one-half its size. The original growth was composed of stratified squamous epithelium, with occasional leukocyte and hyalin cell inclusions. The subepithelial tissue was a loose fibrous stroma, thickly infiltrated with cells, mostly of connective-tissue type; also there were some lymphocytes and plasma cells, and occasionally polymorphonuclear leukocytes. Among these two processes were foci of larger cells of the epithelial type, but without definite arrangement. Some portions of the growth suggested the cells which are seen in sarcoma, but on the whole, the picture appeared to be best explained as representing an inflammatory rather than a neoplastic tissue. Later additional studies, in view of the return, suggested that the inclusion of epithelial cells previously described should be regarded as an early invading epithelioma.

The authors reviewed some of the literature of epibulbar growths, with special reference to the conclusions reached by Verhoeff and Loring, and thought that the interest attaching to this growth resided largely in the history which had been detailed, the primary disappearance after cauterization, the period of time which followed its removal before its return became evident, and the effect of radium.

They also detailed the history of a small pigment mass, situated 1 mm. from the corneal margin, on the outer side, 1.5 mm. in length and 1 mm. in breadth, upon a vascularized base. This had existed for ten years in the eye of a woman, aged twenty-five years, unchanged, but was said to have begun to grow one year prior to her examination. It was dissected from its base, and the pigmented area found to be closely attached to the corneoscleral margin.

Sections showed that the epithelium was reduced to a single layer of cells. In the subepithelial tissue there was a mass of pigment surrounded by numerous small round cells of the polymorphous type. Other fields showed the presence of both spindle and

round cells and the bloodvessels had well-marked muscle walls, and several capillaries were filled with small round cells, suggesting that extension at this point had commenced. The appearances were those of melanotic round-cell sarcoma.

That epibulbar sarcomas may develop from collections of pigmented cells on the conjunctiva, the so-called melanomas, is well known, and in a subsequent discussion of the pathological appearances it was suggested by Dr. Shumway that the growth should be considered as a nevus pigmentosus, which also, as was pointed out by Wintersteiner, may give rise to sarcoma.

Dr. Risley, in discussing Dr. de Schweinitz's paper, said that for many years he had regarded the corneal limbus as a dangerous surgical area. The first case presented by the essayist, which Dr. Risley had himself seen eight months before, he remembered having used as a text in a clinical talk to students, and urged the possible serious import of disease at the corneal limbus. An ulcer or injury only a millimeter or two removed on to the cornea itself would rapidly recover; or if the injury or disease were in the conjunctiva of the ball a few millimeters from the limbus, he usually felt no apprehension as to the recovery, but in this narrow zone at the limbus he thought most experienced surgeons were apprehensive of a more serious sequel. He thought this might find explanation in the somewhat peculiar histological condition found in the zone between the scleral roll or ring and the limit of the two basal tissues of the cornea, viz., the membrane of Bowman and the membrane of Descemet, in which the sclera merges into the corneal stroma and the conjunctiva into the epithelium of the cornea.

Anophthalmia

Dr. T. B. Holloway exhibited two children with anophthalmia, who were students at the Overbrook Institute for the Instruction of the Blind. In each case the records failed to show a history of any hereditary taint or consanguinity. There were no other abnormalities. In all four orbits the pulley of the superior oblique

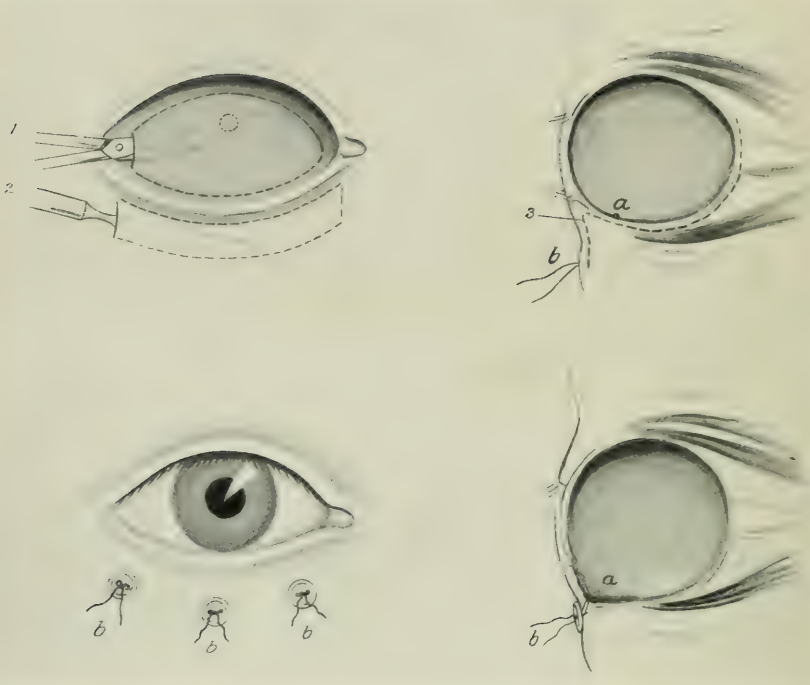
muscle could be distinctly felt. No stigmata of inherited specific disease were present.

Case I.—Female; white; aged nine years. Birth normal. Congenital defect noted by the mother two days after birth. Since the birth of the patient the mother has had three children: one died at the age of three months, probably as the result of marasmus; the other two are healthy, robust children. The length of the palpebral fissures was 14 mm. The right socket was partially divided by a somewhat constricting band of conjunctival tissue extending from the outer extremity of the palpebral fissure to the inner portion of the upper lid just back of the punctum. The upper pocket was the deeper, and while no nodule could be seen, lateral and vertical movements of the apex were noted. The same conjunctival conditions existed within the left orbit. The puncti were present on both sides. The tip of the little finger could barely be introduced within each orbital cavity, and there appears to have been some condensation of tissue at the apex, although this could not be outlined as a definite globular mass.

Case II.—Male; colored; aged nine years. The condition was noted by the mother three days after birth, at which time an oculist called in consultation said the child was born without eyes. The mother has had two other children: one died of diphtheria, the other of "spasms," aged three years and eight months respectively.

The palpebral fissures measured 13 mm. The puncti were present on both sides. The right socket had the same constricting band running horizontally across the orbit as in Case I, but the band was not as marked, and terminated about half-way between the apex and the internal canthus. No globular mass could be seen. With the finger inserted into the orbit no nodule could be felt. The left showed conditions identical with those described for the right eye, except that there could be noted a suggestion of a very small globular mass beneath the conjunctiva, noted particularly by its rotation in various directions. With the finger inserted into the orbit it likewise could be felt.

In reply to Dr. Buchanan, Dr. Holloway stated that a Wassermann test had not been made in either case.



Original Operation for the Restoration of the Socket.

DECEMBER 16

Original Operation for the Restoration of the Socket

Dr. P. N. K. Schwenk presented a case on which he had done an operation for restoring the cul-de-sac after a method of his own.

While working in a bottling establishment ten years ago the patient was struck in his right eye by fragments of an exploding mineral water bottle, necessitating enucleation. He wore a glass eye until six months ago, when it could no longer be retained because of cicatricial contractions and granulations. He consulted Dr. William Pancoast, who removed the granulomata and referred the case to Dr. Schwenk, who admitted him to the Wills Hospital six weeks ago with a view to performing a Maxwell operation. There was a redundant conjunctiva with lower lid everted, and rather deep orbit.

After careful study of the case the following operation was decided upon: The conjunctiva was undermined and brought forward, doubled upon itself to form a new cul-de-sac. To do this the conjunctiva was entirely loosened from the floor of the orbit from a point just below the margin of the lower lid to a point 3 or 4 mm. above the nerve head, by means of scissors, curved on the flat, entrance being made at the outer canthus. A transverse band of skin about 6 mm. wide, having its upper limits 3 mm. from the lid margin, was undermined from canthus to canthus by means of a Graefe knife inserted at the temporal side. By means of the scissors the remaining tissues of the lid were then cut through transversely into this subcutaneous pocket at a point 3 mm. from the lid margin, thus increasing the depth of the orbital cavity by an amount equal to the depth of the subcutaneous dissection. Three double-armed heavy silk mattress sutures were inserted in the loosened conjunctiva from above at a point 7 mm. from its attachment at the lid margin and the needles were carried into the subcutaneous cavity, where they were passed out through the skin at its lower part and tied on Ziegler pearl buttons; a gold conformer was then inserted.

Considerable hemorrhage resulted from cutting the hypertrophied conjunctiva, but there was no subcutaneous ecchymosis, and healing resulted without undue reaction. The stitches were allowed to remain seven days when the conformer was replaced by a glass eye.

Dr. Schwenk stated that this operation is indicated in cases in which the conjunctiva is sufficiently redundant to allow of its being slipped into the anterior cavity and has the advantage of leaving neither deformity nor raw surfaces, as all cutting is done beneath skin and conjunctiva.

Dr. Ziegler asked Dr. Schwenk how his operation differed from the Weiner operation.

In reply Dr. Schwenk stated that Weiner dissected a large flap of conjunctiva from the floor of the orbit up to the margin of the lower lid, then loosened the skin of the lid and pushed the flap into the cavity made by the skin dissection, thus leaving a large denuded surface from which the conjunctiva had been taken. This he covered with either Wolfe or Thiersch grafts and applied a conformer until socket was quiet. In the author's operation no raw surfaces were left to be covered.

Multiple Rupture of Choroid

Dr. Frederick Krauss presented a case of multiple rupture of the choroid resulting from a brick striking the eyeball and outer rim of orbit. There were five distinct ruptures, the largest near the temporal side of the disk, had the shape of a somewhat triangular crescent; one was horizontal, below the disk and three others which were in the form of long, narrow crescents were vertically placed beyond the macula.

Is Immediate Magnet Extraction Justifiable without Localization?

Dr. S. D. Risley described the case of a young man, aged seventeen years, who had been assigned to his clinic at the Wills Hos-

pital three hours after receiving a foreign body in the left eye while acting as a foundryman's helper. The foreign body entered at the nasal corneal limbus; there was no pain, but the eye was blind and there was no light reflex from the fundus. The recent occurrence of the injury, the location of the still open wound of entrance, suggested the inquiry "Is an immediate attempt at extraction of the foreign body with the magnet without waiting for its localization advisable? If not, why not?" As this inquiry was under discussion before a class of students, Dr. William M. Sweet entered the clinic room and said he did not think it advisable, without a knowledge of its location, size, and form; that if it chanced to be a long sliver of metal it was quite as likely to approach the wound of entrance sidewise as endwise. Dr. Risley recalled an example where this had occurred in his own experience, the wound of entrance being in the ciliary region. Failing to extract the metal, the ball was enucleated a few days later and a fine strip of metal 7 mm. long by 1 mm. and 1½ mm. in diameter was found lying across the wound of entrance in the ciliary region, where it had apparently been drawn by the magnet. Then, too, in case the body were situated deeply in the globe, less injury to the ciliary region would be inflicted by withdrawing it through a scleral puncture made as near as possible to the known site of the foreign body, as ascertained by localization.

In addition to the accurate localization of the foreign body, another, and a very important, objection to immediate magnetic extraction was the unknown size and weight. While the weight cannot be determined, it can be estimated with relative accuracy by the size. Dr. Risley had seen a metallic fragment which weighed 2½ grains fly from the eye through the corneal wound, dragging with it a considerable segment of the iris and fastening itself upon the tip of the Haab magnet when the instrument was not within eight, or possibly ten, inches from the cornea. A careful localization and determined size of the body would have made it possible to avoid this unfortunate accident and the violent pain it occasioned.

In discussing Dr. Risley's paper, Dr. Sweet stated that the

magnet should not be used unless the operator had a knowledge of the size of the metal in the eye and its approximate location, except possibly where the wound of entrance, still open, was in the sclera back of the ciliary body. The size and situation of the opening made by the foreign body could not be depended upon to indicate its probable shape and location. A long, thin piece of steel enters the globe through a small wound similar to that made by a short, flat particle. The smaller body may pass completely through the eyeball into the orbit, lodge in the posterior portion of the globe, or drop immediately behind the ciliary body. A strong magnet applied at the entrance wound will not secure the long, thin piece of metal, and may cause a small body, particularly if irregular in shape, to become imbedded in the internal structures, particularly the ciliary body. He recalled two cases in which the magnet point at the entrance wound in the lower portion of the cornea failed to secure the foreign body. Subsequent *x*-ray localization showed the steel, one piece somewhat broad and irregular in shape and the other moderately long and narrow, to have been drawn forward and become imbedded in the ciliary body. In both instances the injured eye was subsequently lost. In another case, the operator failing to secure the steel through the open entrance wound, incised the sclera back of the ciliary body, but failed to remove the metal. An *x*-ray examination made later showed that the steel had passed through the globe into the orbit.

Dr. Krauss stated that he had removed pieces of steel from the eye in cases where the *x*-ray plate could not be obtained quickly. In one case of an exceedingly fine linear piece of steel which did not appear on the *x*-ray plate, the magnet successfully removed it through a second incision in the cornea. This was found necessary when the glistening of a minute body in the anterior chamber at right angles to the plane of the cornea was evident, after the use of the magnet in the anterior chamber.

Dr. Ring emphasized the importance of not only having accurate localization of a foreign body, but also a knowledge of its size.

Ten days ago Dr. Ring was called to see a man, aged thirty-five years, who two hours before was struck in the right eye with what proved to be a piece of steel; it passed through the lens, nicking the upper and outer pupillary edge of the iris and at the time of examination the lens was swelling rapidly. An *x*-ray taken a few hours later revealed the presence of a foreign body in the vitreous 11 mm. from the pole of the cornea, 5 mm. below and 1 mm. to nasal side.

The eyeball was opened the following day at a point about midway between the internal and inferior recti and sufficiently far back from the ciliary border. The opening was made with a narrow Graefe knife, and the conical point of the magnet was applied to the point of incision. It was easy to recognize the drawing of the foreign body toward the magnet, but it did not appear, hence the wound was slightly enlarged, the magnet reapplied and the foreign body at once removed. If the measurements are accurately given the matter of the incision is a very simple one, but in this particular instance the *x*-ray expert failed to give the size, hence the necessity for enlargement of the original incision.

Dr. Zentmayer asked Dr. Sweet whether under certain circumstances he would not modify the dictum he had just pronounced? If the accident occurred in a place so located that to have a radiograph taken would mean a delay of perhaps forty-eight hours or more, would not the resulting danger of infection or throwing out of exudate more than offset the advantage of an accurate localization.

Dr. Sweet said that while accurate localization of foreign bodies might not be possible in regions remote from the large industrial centres, the hospitals in all the smaller cities are equipped with adequate *x*-ray apparatus, and many with facilities for general stereoscopic work, so that the exact size of the body in the eye, and some idea of its situation, may be determined before an operation for its extraction is attempted. A skilled *x*-ray worker, without special localizing apparatus, may indicate roughly the situation of the steel from a study of the corneal shadow and the stereoscopic plates of the orbital region. If the plates show the body

to be of small size, extraction may be attempted with the magnet at the open wound, or with the point opposite the centre of the cornea in the hope of drawing the steel around the lens into the anterior chamber. Should the foreign body not come forward, the operator may consider the advisability of making an incision in the sclera, between the external and inferior recti muscles, and endeavor to secure the metal with the magnet point at the opening made but not entered into the vitreous. If unsuccessful, however, it complicates any later operative procedure that may be required after exact localization. Patients who are not seen until several days after injury, at which time the entrance wound will have healed, should have an accurate localization of the metal before extraction is attempted. The delay of a few days is of less importance than the risk of an unsuccessful operation, and the necessity of a subsequent attempt at extraction after the situation of the body has been determined.

A Note on Ethylhydrocuprein

Dr. Howard F. Hansell alluded to the literature of the past two years since ethylhydrocuprein was first used in ophthalmology. He described the following case by which the remarkable effect of ethylhydrocuprein in pneumococcus inflammations is well illustrated:

Case I.—The first time Dr. Hansell saw this little girl of three years was at the end of her convalescence from measles. She was in the children's ward for contagious diseases at the Philadelphia General Hospital. The measles had not been unusually severe, had run its regular course, and was unattended by any complication with the exception of an inflammation of the lid and cornea of the left eye. The conjunctiva was intensely red and edematous, the lid swollen to such a degree that it was difficult to evert it. The discharge was abundant and contained numerous pneumococci. The culture showed no admixture of other cocci. The lower, outer third of the cornea was necrotic, the process extending laterally to include other portions of clear cornea, and deeply, to invade fully one-half of the layers of the cornea. The necrotic

masses were easily wiped away with a wad of cotton, exposing a gray, uneven base. Ethylhydrocuprein, 1 per cent., was ordered to be instilled every two hours, day and night, and the eye frequently flushed with a weak solution of bichloride of mercury. In twenty-four hours great improvement was evident. The process of ulceration had been checked, the discharge lessened, and the conjunctiva and lids were much less inflamed. At the end of twenty-four hours more the eye was practically well and the child was discharged from the hospital. At the last inspection new tissue had replaced that destroyed by ulceration, the boundary line between the opaque and clear cornea was sharply defined and the lids and conjunctiva had regained their normal appearance.

Dr. Zentmayer stated that he would like to place on record the notes of 8 cases of infected corneal ulcer, all but 1 of which were produced by the pneumococcus; also 1 case of pneumococcus conjunctivitis treated with *optochin*. They were all treated after the manner advised by Kummell. In the series were cases illustrating points brought out by previous reports. There was a case associated with dacryocystitis. The eyeball was saved and the sac infection cured. One case illustrated the point made by Leber that a relapse may occur which is less amenable to the drug than at the beginning of the inflammation. The results could hardly be said to be brilliant, though they seemed better than secured by other methods without ethylhydrocuprein.

Case II.—Admitted three days after being struck in eye by a piece of rock. Large sloughing ulcer with hypopyon. Ulcer cauterized on admission. Ethylhydrocuprein first used on third day. On fifth day a Saemisch was done. On the seventeenth day the ulcer was clean and a roller bandage was ordered. Discharged on thirty-seventh day.

Case III.—Admitted two weeks after injury of the eye with a blade of grass. Pneumococcic ulcer with hypopyon. Optochin from first day. On eighth day slight increase of infiltration. On the fourteenth day cauterized with trichloracetic acid. Discharged one month from admission with ulcer healed.

Case IV.—Admitted one week after beginning of inflammation. No history of trauma. Had similar trouble one year ago. Got well without treatment. (Patient's statement.) Pneumococcic ulcer with hypopyon. Optochin first used on second day. On fifth day hypopyon absorbed. On eighth day ulcer clear. Discharged on twentieth day, ulcer healed V. = 8/30.

Case V.—Admitted nine days after coal injury. Large pneumococcic ulcer with hypopyon. Dacryocystitis. Optochin from first day. On sixth day ulcer cauterized, with trichloracetic acid. Optochin stopped one week. On twenty-first day paracentesis performed. On the thirty-third day descemetocele. Discharged on forty-fifth day. Eye quiet. Cornea flat.

Case VI.—Admitted three months after inflammation began. No history of trauma. Lower half of cornea involved in ulcer. Hypopyon T. + 1. Optochin used from start. Second day ulcer cauterized. On fifth day ulcer perforated. Discharged on ninth day. Ulcer healing.

Case VII.—Admitted on twenty-sixth day after coal injury. Small pneumococcic ulcer with hypopyon. Optochin from start. Discharged on seventh day; ulcer healed.

Case VIII.—Admitted sixteen days after injury by piece of iron. Treated by an oculist until time of admission. Large pneumococcic ulcer involving middle two-thirds of cornea; deep hypopyon. Cicatricial ectropion of both lids from burn of face in childhood. On twenty-third day actual cautery applied to ulcer and base perforated. Optochin from start. Discharged at the end of six weeks with adherent cicatrix. Clear corneal tissue above.

Case IX.—Admitted three weeks after injury by coal. Incipient panophthalmitis. Ulceration extended to Descemet's membrane. Smear negative. Optochin from start. On sixth day ulcer margins lightly touched with carbolic acid. Thirteenth day eye much more quiet. T. + 1. Discharged on eighteenth day cornea flat. V. = hand movements.

Case X.—(Pneumococcic conjunctivitis.) Three weeks before admission had an attack of catarrhal conjunctivitis. On admission had a pneumococcus conjunctivitis. Optochin from start.

On fourth day organisms had disappeared. On sixth day cataract extraction. Healing without incident.

Dr. Ring said that in the use of ethylhydrocuprein his experience was limited largely to its use in pneumococcic chronic dacrocystitis, the effect of a 2 per cent. solution was exceedingly prompt in temporarily clearing up the suppurative condition, but as the result of its application the patient complained so severely of the pain that it had to be reduced to the 1 per cent. solution, and as that could not be used beyond a few applications for the same reason, the good effect noted was, while striking, only temporary.

Dr. Risley had used this drug in a severe case of pneumococcic infection which illustrated one possible cause for the relapse during the use of the drug, a fact which had been pointed out by Dr. Hansell.

A boy, aged eight years, having passed the crisis in a severe attack of pneumonia, was suddenly attacked by pain and injection of both eyes with impaired vision. Notwithstanding the efforts of the physician and a consulting ophthalmologist, the disease rapidly advanced to the destruction of both eyes. When seen at Dr. Risley's Wills clinic the child was ashy pale and his general condition critical. The eyelids were swollen, the tarsal conjunctiva covered with redundant granulation masses and others projecting through the ruptured cornea. There was a profuse discharge of creamy-white pus. The laboratory report revealed an abundant pneumococcic infection with a few streptococci. The child was admitted to the hospital, cold compresses continuously applied, and after thorough washing a 2 per cent. solution of optochin was freely instilled every two hours. The improvement was rapid and marked, then ceased, and the eyes became worse. A second laboratory study then showed an almost complete absence of pneumococci, but a virulent streptococcic infection.

Two Cases of Sarcoma of the Choroid

Dr. Edward A. Shumway reported 2 cases of sarcoma of the choroid, exhibiting sections for microscopical study. One was a

melanotic, spindle-celled growth, which occurred in a man seventy-three years of age, in an eye which had been blind for twenty years, as the result of a blow on the head. The tumor was a large one, which filled nearly the entire eyeball, and had caused severe iridocyclitis and secondary glaucoma. The second was an unpigmented endothelioma, which had developed in the eye of a colored woman, thirty-two years old. Instead of breaking through the lamina vitrea of the choroid, it had spread laterally, invading the sclera, and had broken through into the orbit, so that exenteration of the contents of the orbit had been necessary. Dr. Shumway called attention to the important difference in the manner of growth of these two forms of choroidal tumors, one leading to metastasis elsewhere, the other to early invasion of the orbit, and more probable local recurrence.

A Note on the Rectal Administration of Ether

Dr. P. N. K. Schwenk stated that he had under his care a man, seventy-six years of age, whose vitality was so reduced that the administration of ether in the usual manner was counterindicated. He had nasal *polypi* and sarcoma of the orbit. One hour before operation he was given the following per rectum:

Morphia sulph. gr. $\frac{1}{4}$, paraldehyde f℥ij, ether f℥iv, and olive oil f℥iv, followed half an hour later by a mixture of ether and olive oil, equal parts. Six ounces of this latter mixture was all the bowel would retain.

When the time came for the operation the patient was still conscious, so a solution of novocain was injected into the orbital tissues. The entire orbital contents were resected and the ethmoid and part of the antrum were cleaned out, after which the patient fell asleep and suffered no inconvenience from the ether, the pulse and respiration remaining undisturbed. Above all there was freedom from the shock so common in old people following ether.

Bilateral Exophthalmos Probably Due to Cerebral Aneurysm

Dr. Frederick Krauss presented a case of bilateral exophthalmos, which later became a unilateral pulsating exophthalmos, probably due to cerebral aneurysm. The patient, fifty-seven years of age, with a blood-pressure of 202 systolic, showed enormous bilateral exophthalmos, more marked on the right side. There was no pulsation, but an enormous bruit was heard all over the head, being loudest over the temporal bone. The bruit was continuous but accentuated with each cardiac impulse, and ceased after compression of the common carotid.

After a partial subsidence on the right side and complete on the left, there was a sudden return of the symptoms, especially in the right eye which showed marked pulsations, synchronous with the radial pulse. The syndrome of symptoms indicated an arteriovenous aneurysm forming between the internal carotid and cavernous sinus on the right side. The bruit became loudest over the right eye. There was tremendous exophthalmos in the right eye with complete palsy of all the ocular muscles, including the sphincter iridis which was fully dilated and immobile. Under treatment which included rest in bed and intermittent occlusion of the common carotid artery, the condition improved very greatly. After the second attack the vision fell from $\frac{1}{3}$ vision to absolute blindness. The ophthalmoscopic changes were first dilatation of the veins, retinal hemorrhages, engorgement of the choroidal vessels, edema of the nerve and retina, followed later by low-grade iridocyclitis, with resulting synechia and vitreous opacities.

Dr. Zentmayer stated that there were three symptoms in Dr. Krauss's case which pointed to involvement of the cavernous sinus: (1) Papillitis. It will be recalled that Graefe believed the cause of choked disk to be due to thrombosis of this sinus; and while it has been found that this has not been true in most cases, still in a case reported by Gruening of thrombosis of the cavernous sinus choked disk was present. (2) Bilaterality after a time. (3) Palsy of the extra-ocular muscles.

Congenital Cataract and Coloboma of Iris in Mother and Child

Dr. G. Oram Ring exhibited two patients, mother and child, showing congenital abnormalities of the iris and lens and gave the history of a second child of the same parents in whom a similar congenital abnormality had been present.

The examination of Mrs. T. R., the mother of four children, two with normal eyes and two showing anomalous development, was as follows:

R. E. Iris below notched or slightly folded upon itself. At posterior pole of lens there was a dense white opacity. Nuclear riders were present and numerous dots of intense whiteness were scattered throughout the lens.

In L. E., a coloboma of iris was present below with similar lens haze. Each eye had microcornea.

In the child exhibited microphthalmos was present in each eye.

In the R. E. there was a posterior polar opacity in the form of an irregularly round nodule, with a number of riders in the nuclear area and several small dot-like opacities scattered throughout lens.

L. E. Similar lens appearance except for absence of area of dot-like haze.

In both eyes the iris showed a concave depression, corresponding in position to the coloboma of the mother.

A second child with a congenital defect died when five months old, but had double microphthalmos, double coloboma and lenticular opacities, the latter similar to those of mother and older child.

Of the two older children the first died at five months of gastroenteritis, and the last child born is living and in good health, neither of the latter had any ocular abnormalities.

The mother whose ocular condition is described above was the fourth of eight children and had a particularly wretched prenatal history, *her* mother being brutally treated even to the point of insufficient food and shelter by a father addicted to excessive alcoholism.

Dr. Ring made reference to the various types of iris abnormalities and their association and quoted the classification of Lang and Collins and the failure of some of the text-books to associate the lens and iris defects was commented upon.

The anatomical appearance of the anterior segment of the eyeball previous to the formation of the iris in fetal life was described.

The relation of the iris to the vascular extensions from the posterior to the anterior fibrovascular sheaths were detailed and reference made to the explanation given by Swanzy of some abnormal adhesion between the corneal anterior fibrovascular sheath and lens capsule, as inducing an obstruction to the proper iris development.

Dr. Ring proposed to operate upon the cataracts in the case of the mother, who was thirty-five years of age, by carefully incising lens capsule and lens with a Hays-Ziegler knife, making the initial incision in the vertical meridian and extending it from the lower to the upper border of the dilated pupil.

Dr. Risley stated that he felt that operation in this case was indicated and should be undertaken.

Dr. Hansell spoke of a family of eight children, three of whom had congenital cataract in each eye, all lamellar. The mother had congenital coloboma of the iris and a high-grade amblyopia in one eye. He had operated on all three children with satisfactory results.

In another family the grandmother had senile cataract. The daughter double congenital lamellar cataract and the grandson also congenital lamellar cataract. One operation had been performed on one eye of the mother and the eye lost before the family came under his observation. Operation on the remaining eye was entirely successful, convalescence having followed the usual course.

George S. Crampton, M.D.,
Clerk.

APPENDIX

ANNUAL REPORT OF THE LIBRARY COMMITTEE FOR 1915

MR. PRESIDENT: In accordance with the ordinances and By-Laws of the College, I herewith submit the following report of the Library Commitee for the year 1915:

Total number of volumes in the Library, including the bound volumes and 10,237 unbound "Reports" and "Transactions"	107,782
Number of unbound "Theses" and "Dissertations" .	12,949
Number of unbound pamphlets	90,670

Included in the above total there are 3,454 volumes known as "reserves," consisting of second copies of some of the more important periodical publications, and 3,010 volumes more or less incomplete.

The duplicates, which are not included in the above total, number 4,899.

The following table shows the number of volumes in the various divisions of the Library:

	Bound.	Incomplete and unbound.	Total.
General Library . . .	77,178	2,963	80,141
Lewis Library	13,586	44	13,630
On permanent deposit:			
S. D. Gross Library . .	3,545	9	3,557
Library of the Obstetrical Society of Philadelphia .	217	..	217
			97,545

Received during the year from all sources 3,724 volumes, 12,522 pamphlets and 20,790 numbers of various periodicals.

Divided as follows:

	Volumes.	Pamphlets.	Journals.
General Library	3,112	12,484	20,790
Lewis Library	11		
S. D. Gross Library	9		
By Purchase from General Fund	288		
In Exchange	304	38	
	3,724	12,522	20,790

Accessions (including 170 volumes "reserves"):

General Library	2,065
Lewis Library	11
S. D. Gross Library	9
	2,085

Total increase in number of volumes for the year, 2,085.

Photographs received in response to requests sent out during the year:

Fellows of the College, 148. Foreign, 79.
Total number of portraits listed, 6,690.

The individual "donors" for the year ending November 1, 1915, number 461; this represents 860 distinct presentations. Each gift is duly acknowledged and properly recorded.

The following list shows the donations of 25 volumes or more, and the number of volumes presented by the various publishing houses:

	Volumes.
Dr. Morris Longstreth	596
Dr. J. S. Gibb	188
Dr. Edward Martin	141
Dr. Charles K. Mills	125
Dr. E. H. Siter	105
Dr. Franklin Mathews	79
Dr. G. S. Crampton	62
Dr. John M. Cruice	59
Dr. William H. Bennett	50
Dr. William W. Keen	48
Dr. John K. Mitchell	45
Dr. H. W. Stelwagon	45
Dr. John T. Carpenter	41
Dr. Hobart A. Hare	41
Dr. Alfred C. Wood	38
Dr. Addinell Hewson	36
Dr. G. E. de Schweinitz	36
Dr. Clarence Hoffman	35
Dr. J. C. Gittings	34
Dr. James C. Wilson	33
Dr. George B. Wood	25

From the publishing houses of:

P. Blakiston's Son & Co.	30
F. A. Davis Company	11
Lea & Febiger	14
J. B. Lippincott Company	20
Longmans, Green & Co.	1
W. B. Saunders Company	59
William Wood & Co.	10

The Library is indebted for large gifts of pamphlets and unbound periodicals to the following donors:

Dr. Oscar H. Allis
Dr. A. P. C. Ashhurst
Dr. John Aulde
Dr. Charles Baum
Dr. William H. Bennett
Messrs. P. Blakiston's Son & Co.
Dr. Henry W. Cattell
Dr. Burton Chance
Dr. John M. Cruice
Dr. Charles H. Frazier
Dr. John S. Gibb
Dr. J. C. Gittings
Dr. E. H. Goodman
Dr. J. P. Crozer Griffith
Dr. Alfred Hand, Jr.
Dr. Hobart A. Hare
Dr. J. Norman Henry
Dr. Addinell Hewson
Dr. Howard K. Hill
Dr. A. Bern Hirsh
Dr. C. J. Jones
Dr. Charles F. Judson
Dr. William W. Keen
Dr. John A. Kolmer
Dr. Theodore LeBoutillier
Dr. Robert G. LeConte
Messrs. J. B. Lippincott Company
Dr. Morris Longstreth
Dr. Edward Martin
Dr. Charles K. Mills
Dr. John K. Mitchell
Dr. Elliston J. Morris
Dr. Charles C. Norris
Dr. Maurice Ostheimer
Dr. John B. Roberts
Messrs. W. B. Saunders Company
Dr. George E. de Schweinitz
Dr. William M. Welch
Dr. Henry R. Wharton
Dr. J. William White
Dr. James C. Wilson
Dr. Alfred C. Wood
Dr. H. C. Wood
Dr. M. W. Zimmerman

574 new publications were added to the Library during the past year. 52 of these were written or edited by Fellows of the College. 24 volumes were presented by the following authors or editors:

Francis G. Benedict, Esq.
Dr. W. M. Brickner (compiler)
Dr. Charles W. Burr (editor)
Dr. Clifford B. Farr
Dr. Martin H. Fischer
Dr. L. F. Frank
Dr. Hobart A. Hare (editor)
Dr. J. C. Hemmeter
Dr. Edward Jackson (editor)
Dr. Thomas McCrae (editor)
Dr. Leon C. Márquez
Dr. J. Ewing Mears
Dr. Francis R. Packard (editor)
Dr. Paul Röthig
Dr. B. Samper
Dr. H. B. Sheffield
Dr. H. A. Vermeulen
Dr. James C. White
Dr. Joseph Leidy

28 volumes were sent by the publishers at the request of the following authors or editors:

Dr. Henry W. Cattell (editor)
Dr. W. A. N. Dorland (editor)
Dr. Edward B. Gleason
Dr. J. P. Crozer Griffith
Dr. Hobart A. Hare
Dr. John A. Kolmer
Dr. D. Braden Kyle
Dr. Henry Leffmann
Dr. Guthrie McConnell
Dr. R. Tait McKenzie
Dr. Charles K. Mills
Dr. Henry Morris
Dr. Charles E. de M. Sajous
Dr. Jay F. Schamberg
Dr. Alfred Stengel
Dr. A. A. Stevens
Dr. Francis T. Stewart
Dr. Benjamin A. Thomas
Dr. James Tyson
Dr. James C. Wilson

Summary of the Funds:

	Volumes purchased.	Cost.
Henrietta Rush Fales Baker Fund	26	$89.19
Luther S. Bent Fund	11	14.65
William T. Carter Fund	28	91.69
Girardus Clarkson Fund	8	25.25
Francis X. Dercum Fund	33	88.85
Louis A. Duhring Fund	4	82.13
John D. Griscom Fund	32	99.63
William F. Jenks Fund	40	116.38
Oliver A. Judson Fund	5	(Paid 1913–1914)
William V. and John M. Keating Fund	13	21.04
William W. Keen Fund	36	72.39
Library Endowment Fund	91	365.81
Horace Magee Memorial Fund	110	362.09
J. Ewing Mears Fund	13	42.24
Charles K. Mills Fund	00	0.00
Wier Mitchell Fund	23	78.62
John H. Musser Fund	5	10.77
Elizabeth K. Newcomet Fund	11	21.88
William F. Norris Fund	18	59.55
Charles A. Oliver Fund	3	6.23
Philadelphia Medical Society Fund	2	9.63
Lewis Rodman Fund	17	47.00
Douglas Stockton Warren Fund	15	39.30
John F. Weightman Fund	7	20.32
Caspar Wistar Fund	20	86.06
	571	$1,850.70

Special Accounts:

	Volumes purchased.	Cost.
Fund for completing files of journals	25	$94.81
Fund for rare and valuable books	15	1,002.91
Journal Association	11	16.09
New Book Fund	8	15.77
S. D. Gross Library Account	5	42.16
	64	$1,171.74

George B. Wood Fund for Library supplies, stationery, etc. Expended, $135.25.

	1915.	1914.	Decrease.
Books bound	953	1813	860

Visitors:

	1915.	1914.	Decrease.
Number of visitors to the Library	8,270	8,469	199
[Fellows of the College	3,263	3,818	555]

The Library has been kept open two evenings each week and on the six minor legal holidays, for the same hours and period of time, as during the preceding year.

	1915 (75 evenings).	1914 (78 evenings).	Increase.
Visitors, evening	690	462	228
[Fellows of the College	186	145	41]
			Decrease.
Visitors, legal holidays	125	154	29
[Fellows of the College	24	49	25]

The above figures are included in the total number of visitors for the year.

	1915.	1914.	Increase.
Number of books consulted in the Library	25,770	24,000	1,770

The number of books reported as "consulted in the Library" includes only those supplied by the Librarian or his assistants. Readers have access to the bound volumes kept in the Reading-room, and the Fellows of the College have access to the Book-

stacks. There are therefore a great many volumes consulted of which no accurate record can be kept.

	1915.	1914.	Increase.
Number of books taken out	4,799	4,301	498

	Works.	Volumes.	Cards written.
Catologuing	815	957	12,028

All the books added to the shelves during the past year, and 136 of the more important pamphlets have been catalogued, and each volume has been accessioned and shelf-listed.

11,946 unbound pamphlets and reprints have been subject-headed and arranged alphabetically by subject, and by author under the subject.

Revision of catalogue: Number of cards revised, typewritten, examined and filed for the year ending November 1, 1915: 13,320.

The revision of the catalogue has been completed as far as the subject "Urotropin" in the second series of the "Index-Catalogue."

The current periodical publications, including "Transactions" and "Reports," received as issued, at this time are received through the following sources:

	American.	Foreign.
Henrietta Rush Fales Baker Fund	0	13
Dr. A. P. Brubaker	1	0
William T. Carter Fund	2	10
Francis X. Dercum Fund	0	12
Louis A. Duhring Fund	1	3
John D. Griscom Fund	2	34
Samuel D. Gross Library Account	0	3
William F. Jenks Fund	2	16
Journal Association	1	7
Oliver A. Judson Fund	0	1
William V. and John M. Keating Fund	0	7
William W. Keen Fund	2	10
Library Endowment Fund	4	105
Horace Magee Fund	0	1
J. Ewing Mears Fund	0	2
Weir Mitchell Fund	1	29
Elizabeth K. Newcomet Fund	0	1
Carried forward	16	254

	American.	Foreign.
Brought forward	16	254
William F. Norris Fund	1	9
Philadelphia Medical Society Fund	0	7
Lewis Rodman Fund	0	13
John F. Weightman Fund	0	4
Caspar Wistar Fund	1	9
By Purchase from General Account	31	367
In Exchange	93	91
Editors	123	20
Publishers	51	1
In addition, current numbers of periodicals are received, at stated intervals, through the courtesy of the editors and editorial staff of the following journals: American Journal of the Medical Sciences, Medical World, Therapeutic Gazette	160	60
	476	835

Total number of periodicals received at this date, 1,311.

New subscriptions added during the past year: American 13; foreign, 41. Total, 54.

We exchange publications with the following schools of medicine:

University of Amsterdam	University of Königsberg
" Basel	" Lausanne
" Berlin	" Leiden
" Bern	" Leipzig
" Bonn	" Liège
" Breslau	" Lund
" Erlangen	" Marburg
" Geneva	" Rostock
" Giessen	" Strassburg
" Göttingen	" Upsala
" Griefswald	" Utrecht
" Halle	" Würzburg
" Heidelberg	" Zurich
" Kiel	
Faculty of Medicine of Bruxelles	
" "	Paris
" "	Toulouse
" "	Yucatan

The above list of exchanges has been allowed to stand, but on account of the conditions in Europe, only the following institutions have been heard from during the year: Amsterdam, Basel, Bern, Leiden, and Lund. Inquiries have been made in regard to the Paris theses for the school year 1913–1914, but up to the present time no satisfactory answer has been received. The Bureau of International Exchanges will deliver parcels only to certain places, according to a printed circular received; in consequence, our "Transactions" for the past year have not been delivered to a number of foreign exchanges. These will be held until conditions are such that our exchange of publications can be resumed.

116 dissertations have been received, and of these 60 were added to the Library during the year.

We have received for the current year ending November 1, 1915, in cash, from the sale of duplicates, $133.23.

We have an exchange, arranged on a cash basis, with two New York dealers, and have received during the past year books and journals valued at $137.00; and have a balance to our credit of $137.42.

During the year we have distributed duplicate books and journals on exchange account to the following:

Boston Medical Library
Denver Medical Library
Medical Library Association
Schuylkill County Medical Society
Washington University Medical Library

Returns have been received from Boston Medical Library, Medical Library Association and the Washington University Medical Library.

With the aid of exchanges, and by purchase from funds appropriated for the purpose by the Library Committee, we have, since November 1, 1914, completed our files of the following journals:

American Journal of Ophthalmology. St. Louis
Deutsche Medizinal-Zeitung. Berlin
Hahnemannian Monthly. Philadelphia
Revue Générale d'Histologie. Paris

Amount of fines collected from November 1, 1914, to November 1, 1915, $37.10.

The following is a list of the rare medical books and works of special interest received during the past year:

Incunabula

[Total number of incunabula at this date, 187.]

Aegidius Columna. [De regimine principum.] Romae, Plannck, 1482. F°. [Hain no. 108.]

Fund for Rare Books.

Albertus Magnus. [Physicorum sive de physico auditu libri octo.] Venetiis, de Forlivio, 1488. F°. [Hain no. 518.]

Fund for Rare Books.

Aristotelis. [Opera graece.] Venetiis, Aldus, 1495–98. 5 vols. F°. [Hain no. 1657.]

A superb copy of the first edition of the work of Aristotle, printed in Greek characters. The value of this work is increased by the fact that it was one of the earliest examples of books printed entirely in Greek characters. Dr. Fielding H. Garrison says: "The greatest scientific name after Hippocrates is that of the 'Master of those who knew' the Asclepiad Aristotle (384–322 B.C.) who gave to medicine the beginnings of zoölogy, comparative anatomy and embryology, and the use of formal logic as an instrument of precision."

Presented by Henry Reed Hatfield, Esq.

Bergomensis, J. P. [Supplementum chronicarum.] [Venetiis], Bernardinus de Banaliis, 1483. F°. [Hain no. 2805.]

Fund for Rare Books.

Ficinus Florentinus, Marsilius. De triplici vita. [Parisiis, Wolf, ca. 1492.] 16°. [Copinger no. 2497.]

Fund for Rare Books.

Firmicus Maternus, Julius. De nativitatibus. Venetiis, Simon de Bevilauqua, 1497. F°. [Hain no. 7121 bis.]

This is a first edition with a good example of a Xylographic Gothic title, and a woodcut printer's device on the last page. This work is quite rare, and, while not medical as a whole, contains much pertaining to medicine.

Presented by Drs. Charles W. Burr and Edward B. Krumbhaar.

Jung, Ambrosius. [Tractatus perutilis de pestilentia ex diversis auctoribus congregatus.] Augsburg, Schonsperger, 1494. 4°. [Hain no. 9473.]

A rare German incunabulum.

Presented by Drs. James M. Anders, Thomas G. Ashton, George M. Boyd, Charles W. Burr, Barton Cooke Hirst, David Riesman, Joseph Sailer, James C. Wilson, George Woodward and Sir William Osler, Bart.

Lactantius Firmianus, L.C. [Opera.] [Venice], 1471. F°. [Hain no. 9809.]

Fund for Rare Books.

Rodericus Sanctius. Bishop of Zamora. [Speculum vitae humanae.] Augsburg, Zainer, 1471. F°. [Hain no. 13940.]

A very rare and beautiful specimen from the first press at Augsburg. This is the earliest dated book in the Library of the College, and, while not a medical work, contains a number of passages relating to medical subjects.

Presented by Drs. George E. de Schweinitz and Richard H. Harte.

Serapion [Joan] the younger. [Liber Serapionis aggregatus in medicinis simplicibus.] Venetiis, Raynaldus de Novimagio, 1479. F°. [Hain no. 14692.]

Fund for Rare Books.

Wirecker, Nigellus. [Speculum stultorum.] [Leipzig, Kachelofen, ca. 1494.] 8°. [Hain no. 16217.]

Fund for Rare Books.

Works of Special Interest

Bayle, Pierre. Dictionnaire historique et critique. 3 ed. Rotterdam, Bohm, 1720. 4 vols. F°.

This bibliographical dictionary is considered Bayle's masterpiece. It was first issued in 1695–97 and has become quite rare.

Presented by Dr. Richard H. Harte.

Brandt, Sebastien. [Stultafera navis.] [Basel, Joh. Bergmann de Olpe, 1505.] 8°.

This book is a Latin version, by Jacobus Locher, of Sebastien Brandt's famous "Das Narrenschiff" (Ship of Fools), which first appeared in 1494. This copy lacks the title page and several pages of text.

Presented by Dr. Edward B. Krumbhaar.

Cardanus, Hieronymus. Metaposcopia. Lutitiae Parisiorum, Jolly, 1658. F°.

This book is quite rare, not having been included in the collected editions of the works of Cardanus.

Presented by Dr. John K. Mitchell.

Carmona, J. Tractatus de peste ac febribus cum particularis. Hispali, Maldonado, [1582]. 24°.

By Purchase.

Clark, James. Treatise on the yellow fever as it appeared in the island of Dominica in the years 1793–4–5–6. London, Murray, 1797.

By Purchase.

Goodall, Charles. The Royal College of Physicians of London. London, Kettilby, 1684. 8°.

Presented by Sir William Osler, Bart.

Ingram, Dale. Historical account of the several plagues that have appeared in the world since 1346. London, Baldwin, 1755. 8°.

Fund for Rare Books.

Mercado, Luiz. Libellus de essentia causis, signis, et curatione febris malignae. Pinciae, D.F. à Corduba, 1574. 24°.

By Purchase.

Pirogoff, N. I. Anatome topographica. Petropoli, Trey, 1859. 5 vols. F°.

Pirogoff, the greatest Russian surgeon of his time, is remembered today by his operation of amputation of the foot—"Pirogoff's amputation;" but his Anatomy, a monumental work of great value, in which frozen sections were first used in the process of illustration, seems almost unknown to the present generation. Complete copies are quite rare.

Fund for Rare Books.

Priestley, Joseph. Directions for impregnating water with fixed air. London, Johnson, 1772.

Presented by Sir William Osler, Bart.

Röslin, Eucharius. Der swangern Frauwen und Heebamen Rosengarten. Argentine, Flach, 1513. 4°.

First edition of the first work printed on obstetrics. This work is based on a manuscript by Moschion, a writer of the second century. The "Rosengarten" was translated into English by Thomas Raynald, under the title "The Birth of Mankynd." The binding is an excellent example of early sixteenth century German work.

Presented by Drs. James M. Anders, Thomas G. Ashton, George M. Boyd, Charles W. Burr, Barton Cooke Hirst, David Riesman, Joseph Sailer, James C. Wilson, George Woodward and Sir William Osler, Bart.

Sophia, Marsiliis de Sancta. Opus aureum ac preclarum, de recenti memoria in luces traditum. Lugduni, 1517. 12°.

Fund for Rare Books.

Other Interesting Additions

Aesculapius. Photograph of a statue.

Presented by Dr. James V. Ingham.

American Association for the Advancement of Science. Silver badge, 1914.

Presented by Dr. W. W. Keen.

Cow-Pock, or the Wonderful Effects of Inoculation. Engraving.

Presented by Miss Mary Lee.

Duhring, Louis A. Portrait in oils by H. H. Breckenridge.

Ordered by Resolution of the College.

La Roche, Réné. Portrait in oils. (Artist unknown.)

Presented by J. Percy Keating, Esq.

Purgation-Calendar, 1453. Facsimile of original, printed in Gutenberg types, in the Bibliothèque Nationale, Paris.

Presented by Dr. Fielding H. Garrison.

Vesalius, Andreas. Engraving of the painting "Vesalius Demonstrating."

In Exchange.

We have also received during the year many interesting and more or less valuable autograph letters.

Through the generosity of Dr. Francis R. Packard, the Library Committee have been enabled to have additional steel cases erected in the "Packard Room" to give much needed space for our growing collection of bound manuscripts.

The figures in the present report show a decrease in the total number of visitors to the Library (199), as well as a decrease in the number of visits made by Fellows of the College (555). On the other hand, there is an increase in the number of books consulted (1770), and an increase in the number of books taken out (498). The "Study-rooms" have been in demand throughout the year, the average number of volumes called for and retained in these rooms being 175, an average increase of 9.

The predictions made last year in regard to the effects of the war in Europe upon this Library, as to the receipt of foreign medical literature, have, we regret to say, been fully verified. Something like two hundred and fifty periodicals have ceased to arrive, while some twenty others are received only at irregular intervals. With a few exceptions, the subscriptions for these journals were paid in advance to our agents in New York, Paris and London, and it is our understanding that the journals will be supplied, or the amount of subscriptions returned; but there is a possibility that we may suffer some loss before all matters are adjusted. Our agents, in response to various complaints, have offered to order subscriptions sent direct from the publishing offices of the journals if we would be responsible for loss in transit. This has not been deemed advisable on account of the difficulty in obtaining missing numbers, some of which, possibly, could not be replaced. Most of the books received during the year, other than English and French, have come through Amsterdam. No dissertations or theses have been received from the war zone, and it is likely that none have been issued.

In comparison with the number of new publications received during the year 1913, for instance, there is a loss of about 90 per cent. of the books published in the French language; about 69 per cent. of the books published in the German language, and about 34 per cent. in the publications of Great Britain.

The effect is also shown indirectly in the decreased totals of several items in this report: number of volumes bound, number of volumes purchased from the "Funds," and the total increase in the number of volumes added to the Library during the year.

With the return to normal conditions in the affairs of Europe we will make an immediate effort to obtain the periodical publications and books that have been issued during the period of disturbance, and, whenever this time occurs, it will make a somewhat unusual call upon the funds in the hands of the Library Committee; so, possibly, this matter should be taken into consideration at the present time. The expenditure for books from the income from the "Funds" has been $1,202.51 less than during 1914.

During the past year the Library Endowment Funds have been increased by the Louis A. Duhring Book Fund, $5,000.00, and the Louis A. Duhring Library Fund, $181,122.02.

Total amount of Library Endowment Funds at this date, $292,318.85.

Respectfully submitted,

WILLIAM J. TAYLOR,
Chairman.

REPORT OF THE SECTION ON OTOLOGY AND LARYNGOLOGY

There are twenty-seven active members.

During the past year eight meetings were held with an average attendance of eleven Fellows and sixteen Guests.

Twenty-seven subjects were presented and discussed.

The officers of the section, elected December 16, 1914, are:

Chairman—Dr. George Morley Marshall.

Clerk—Dr. Benjamin D. Parish.

Executive Committee—Drs. B. Alexander Randall, S. MacCuen Smith, George B. Wood.

List of Papers

December 16, 1914

Dr. Ralph Butler: "Report of a Case with Marked Destruction of Soft Palate and Pharynx." Exhibition of patient.

Dr. Nathan Stauffer: "Report of a Case of Traumatic Dislocation of the Septal Cartilage. Submucous Resection Performed." Exhibition of patient

Dr. F. R. Packard: "An Historical Resume of Some Operative Procedures upon the Nose and Throat."

January 20, 1915

Dr. C. C. Eves: "Demonstration of a Postdiphtheretic Laryngeal Case by Direct Laryngoscopy."

Dr. Lewis Fisher (by invitation): (1) "A Case of Carcinoma of Pharynx and Larynx." Exhibition of patient. (2) "A Case of Intralaryngeal Neoplasm." Exhibition of patient.

Dr. G. Morley Marshall: "Report of a Case of an Odontoma Undergoing Sarcomatous Degeneration."

February 17, 1915

Dr. G. Hudson Makuen: "Exhibition of a Case Demonstrating the Possibilities of Teaching Lip-reading to the Adult Deaf."

Dr. S. MacCuen Smith: "Exhibition of some Postoperative Ear Cases, Including Two Brain Abscess Cases."

Dr. E. B. Gleason and Dr. C. E. Pfahler: "Report of a Case of Fracture of the Petrous Portion of the Temporal Bone." Exhibition of *x*-ray plate.

Dr. George Coates: "Report of Two Cases of Mastoiditis Treated with Vaccines after Operation.

March 17, 1915

Dr. Ralph Butler: "Presentation of a Larynx from a Patient Shown at the January Meeting."

Dr. G. Hudson Makuen: "Has the Faucial Tonsil a Capsule?"

Dr. George C. Stout: "A Suggestion as to Eustachean Medication."

Dr. George B. Wood: "The Report of Two Cases of Impacted Foreign Bodies in the Upper Respiratory Tract."

April 21, 1915

Dr. B. A. Randall: "The Anatomy and Physiology of the Static Labyrinth, with Lantern Slide Demonstration."

Dr. Isaac H. Jones: "Demonstration of the Barany Pointing Reactions and Conclusions Drawn from Over One Hundred Cases Examined."

Dr. T. H. Weisenburg: "The Value of an Ear Examination to the Neurologist, with Special Reference to the Barany Reactions."

May 19, 1915

Dr. E. B. Gleason: "Exhibition of Specimen of Necrosis of the Sphenoid and Palate Bones." Exhibition of specimen showing hyperkeratosis of the plica triangularis.

Dr. B. Alexander Randall: "Report of a Case of Double Mastoid Tubercular Caries Complicated by Measles, Nephritis, and Pneumonia with Recovery."

Dr. George M. Coates and Dr. Nathaniel Ginsburg (by invitation): "Report of a Case of Ludwig's Angina Complicating Peritonsillar Abscess." Presentation of patient.

Dr. James A. Babbitt: "The Correction of an External Nasal Deformity by the Rib Resection Method." Exhibition of patient.

Dr. I. H. Jones and Dr. Lewis Fisher (by invitation): "Correction of External Deformity of the Nose." Photograph before operation, and presentation of patient.

October 20, 1915

Dr. E. B. Gleason: (1) "A Case of Cholesteatoma of the Mastoid Antrum and Cells of Many Years' Duration." (2) "A Case of Radical Mastoid on a Patient with a Dead Labyrinth and Serous Meningitis."

Dr. F. R. Packard: "The Report of the Removal of an Inner Tracheotomy Tube from the Lung by Direct Bronchoscopy."

Dr. Geo. B. Wood: "The Report of a Case of Fracture of the Larynx." Exhibition of the patient.

Dr. Lewis Fisher (by invitation): "A Case of Temperosphenoidal Abscess Simulating Cerebrospinal Meningitis." Operation and recovery.

November 17, 1915

Dr. Dudley Guilford (by invitation): "A Lantern Talk on the American Ambulance, showing some End Results of the Treatment of Gunshot Wounds of the Face and Jaws."

Benjamin D. Parish,
Clerk.

REPORT OF THE SECTION ON GENERAL MEDICINE

The Clerk of the Section respectfully submits the following report in accordance with the By-laws of the College. During the year eight regular meetings were held. At the December meeting Dr. Alfred E. Cohn, of the Rockefeller Institute in New York, was the guest of honor. The subject of his paper was "Clinical and Electrocardiographic Studies on the Action of Digitalis." The remaining fifty papers—of which a list is appended—were read by members of the College or local physicians (by invitation). The May meeting was held at the Philadelphia General Hospital.

The total attendance at the eight meetings was 450; the average attendance was therefore 56. The average attendance of members of the Section was 18. These figures show a gratifying increase of interest in the work of the Section on the part of outsiders.

The membership of the Section on November 30, 1915, was 80, as compared with 82 last year. The attention of new members of the College is called to the Rules of the Sections which provide that "Every Fellow of the College who shall send his name for this purpose to the Clerk of a Section shall be a member of it, upon payment of the annual dues of the Section."

List of Papers

December, 1914

Recent Changes in our Concept of the Action of Digitalis. By Dr. H. C. Wood, Jr.

Clinical and Electrocardiographic Studies on the Action of Digitalis. By Dr. Alfred E. Cohn, of the Hospital of the Rockefeller Institute.

January, 1915

Addison's Disease in a Negro with Involvement of the Central Nervous System. By Dr. Alfred Gordon.

Some Visceral Symptoms of Autonomic Disturbance. By Dr. S. Solis Cohen.

Splanchnic Neurasthenia and Its Treatment. By Dr. A. Bern Hirsh.

The Graham-Steell Murmur. By Dr. Joseph Sailer.

February, 1915

The von Noorden Treatment of Diabetes Mellitus. By Dr. James Tyson.

The Diagnosis of Enteroliths by Means of the Roentgen Rays, with the Report of a Case. By Dr. C. E. Pfahler and (by invitation) C. J. Stamm.

Studies in Renal Function with Special Reference to Non-coagulable Nitrogen and Sugar Concentration in the Blood, Phthalein Elimination, and Blood-pressure. By Dr. A. H. Hopkins and Dr. Leon Jonas (by invitation).

(1) A Wider Application of the Widal Reaction. (2) Serous Meningitis. By Dr. W. E. Robertson.

Pectoral Abscess. By Dr. David Riesman.

March, 1915

The Human Hand as an Index of Occupation and Disease. By Dr. G. W. Norris.

Methods the Clinician should use in the Study of Anemia and Jaundice Associated with Enlarged Spleen. By Dr. R. M. Pearce.

Splenectomy in a Case of Pernicious Anemia. By J. E. Talley and J. H. Jopson.

Splenectomy in a Case of Splenomegaly with Hemolytic Jaundice. By Dr. S. McC. Hamill and Dr. C. H. Frazier.

A Case of Obscure Anemia with Splenectomy. By Dr. Alfred Stengel.

Polycythemia with Splenomegaly. By Dr. Joseph Sailer.

A Case of Myelogenous Leukemia Treated by Benzol. By Dr. O. H. Petty (by invitation).

April, 1915

Solitary Abscess (Amebic?) of the Left Lobe of the Liver Cured by Operation. By Dr. C. B. Farr and Dr. J. H. Jopson.

Old Ecchinococcus Cyst of the Liver Simulating Gallstones; Operation and Demonstration of Hooklets. By Dr. J. B. Talley and Dr. J. H. Jopson.

Two Cases of New Growth of the Thymus Gland. By Dr. E. J. G. Beardsley.

Factors Contributing to the Diminished Vocal Resonance of Pleural Effusions. By Dr. C. M. Montgomery.

Studies in Hypersecretion. By Dr. M. E. Rehfuss (by invitation).

Blood and Urinary Nitrogen Curves after Feeding. By Dr. O. H. P. Pepper and Dr. J. H. Austin.

Some of the Factors Underlying the Development of Graves's Disease with Remarks on Vascular Occlusions of the Thyroid Vessels. By Dr. N. Ginsburg.

May, 1915

(Meeting held in the Amphitheatre of the Philadelphia General Hospital.)

Presentation of Cases

(1) A Case Illustrating the Signs of Status Lymphaticus. (2) A Case of Pituitary Disease. By Dr. Joseph Sailer.

A Case of Diabetes Insipidus. By Dr. R. G. Torrey.

(1) A Case under Treatment for Rabies. (2) Gangrene of Both Hands following Erysipelas. (3) Tubercular Peritonitis. Recovery after Tapping. Organism found in Exudate. (4) Cirrhosis of the Liver with Ascites. Recovery after Thirty-six Tappings. By Dr. David Riesman and Dr. C. B. Farr.

Two Cases of Severe Osteo-arthritis Deformans with Ankylosis. Improvement under the Use of Radium Emanation Water. By Dr. S. Solis Cohen and (by invitation) Dr. D. W. Kramer.

A Case of Streptococcic Arthritis Successfully Treated by Autogenous Vaccines. By Dr. Joseph McIver (by invitation).

Papers and Case Reports

The Differences Between a Hypertrophied and a Strong Heart. By Dr. R. N. Willson.

An Unusual Case of Cerebrospinal Meningitis. By Dr. J. N. Henry.

Report of a Case of Sarcoma of the Lung. By Dr. A. P. Francine and (by invitation) Dr. J. W. Morgan.

A Case of Scurvy with Amebæ in the Gums. By Dr. H. D. Jump and Dr. T. M. Tyson.

Report of a Case of Empyema of the Apex of the Pleura. By Dr. H. B. Allyn.

A Case of Multiple Serositis with Autopsy Specimens. By Dr. F. C. Narr (by invitation).

A Case of Gelatinous Carcinoma of the Rectum with Extensive Peritoneal Metastasis. By Dr. R. S. Boles and Dr. S. Marks (by invitation).

The Exciting of the Cardiac Reflex in the Treatment of Enlarged Heart and Aorta. By Dr. M. Solis Cohen.

October, 1915

A Case of Tabes Dorsalis with Painless Gastric Crises. By Dr. G. V. Emerson and Dr. F. D. Wilson (by invitation).

A Case of Asthma Treated by Vaccines. By Dr. T. G. Schnabel (by invitation).

The Use of the Allen Treatment in Diabetes. By Dr. Alfred Stengel, Dr. J. H. Austin, and (by invitation) Dr. Leon Jonas.

Severe Types of Temporary Cardiac Arrhythmia. By Dr. E. B. Krumbhaar.

Intrathecal Intracranial Injections of Autoneosalvarsanized Serum for Unusually Severe and Persistent Headache of Syphilitic Origin. By Dr. Alfred Gordon.

November, 1915

Experimental Studies of Soluble Radium Salts in Organic Nervous Disease. By Alfred Gordon.

The Action of Opium and Its Derivatives upon the Gastro-intestinal Tract of Man, as Shown by Roentgen Ray Studies. By Dr. H. K. Pancoast and Dr. A. H. Hopkins.

The Occurrence of Lobar Pneumonia as a Complication of Pulmonary Tuberculosis. By Dr. H. R. M. Landis.

(1) An Audible Bruit over the Eyeballs in Exophthalmic Goitre. (2) An Eye Symptom (Intra-ocular Hypotension) in Diabetic Coma. By Dr. David Riesman.

Clifford B. Farr,
Clerk.

LIST OF PRIZES AND LECTURES

THE WILLIAM F. JENKS MEMORIAL PRIZE

(Triennial)

1889	John Strahan, M.D.	Belfast (Ireland).
1895	Abram Brothers, M.D.	New York.

NOTE—June 12, 1900, the William F. Jenks Memorial Prize Fund was transferred to the Library as the "William F. Jenks Memorial Library Fund."

ALVARENGA PRIZE OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA

(Annual)

1890	R. W. Philip, M.D.	Edinburgh (Scotland).
1891	L. Duncan Bulkley, M.D.	New York.
1892	R. H. L. Bibb, M.D.	Saltillo.
1894	G. E. de Schweinitz, M.D.	Philadelphia.
1895	Guy Hinsdale, M.D.	Philadelphia.
1897	Joseph Collins, M.D.	New York.
1898	S. A. Knopf, M.D.	New York.
1899	Robert Randolph, M.D.	Baltimore.
1900	David de Beck, M.D.	Cincinnati.
1901	George W. Crile, M.D.	Cleveland.
1903	William S. Carter, M.D.	Galveston.
1905	D. Chalmers Watson, M.D.	Edinburgh (Scotland).
1907	William Louis Chapman, M.D.	Providence.
1908	William T. Shoemaker, M.D.	Philadelphia.
1910	M. Katzenstein, M.D.	Berlin (Germany).
1911	Francis D. Patterson, M.D.	Philadelphia.
1914	H. B. Sheffield, M.D.	New York.
1915	J. E. Sweet, M.D.	Philadelphia.

NATHAN LEWIS HATFIELD PRIZE FOR ORIGINAL RESEARCH IN MEDICINE

(Triennial)

1901	Henry F. Harris, M.D.	Atlanta.
1909	Martin Henry Fischer, M.D.	Oakland.

NOTE.—November 29, 1913, by Supplemental Deed of Trust, the title of this Fund was changed to "Nathan Lewis Hatfield Prize and Lectureship."

WEIR MITCHELL LECTURES

Jan. 17, 1911	Arthur R. Cushny, M.D.	London.
Mar. 30, 1911	Edmund B. Wilson, PhD., LL.D.	New York.
May 16, 1911	Svante Arrhenius	Stockholm.
Nov. 3, 1911	William T. Porter, M.D.	Boston.
Mar. 29, 1912	William H. Howell, M.D.	Baltimore.
Oct. 21, 1912	G. H. F. Nuttall, F.R.S., M.D.	Cambridge (England).
April 4, 1913	H. P. Armsby, Ph.D., LL.D.	Pennsylvania.
Feb. 25, 1914	Harvey Cushing, M.D.	Boston.

PUBLIC LECTURES

Feb. 16, 1910	S. Weir Mitchell, M.D.	Philadelphia.
Nov. 17, 1910	Simon Flexner, M.D.	New York.
Dec. 15, 1910	William H. Welch, M.D.	Baltimore.
April 18, 1911	James G. Mumford, M.D.	Clifton Springs, N. Y.
Nov. 20, 1911	Talcott Williams, A.M., LL.D., Litt.D.	Philadelphia.
April 29, 1912	Owen Wister, A.M., LL.D.,	Philadelphia.
Feb. 17, 1913	John K. Mitchell, M.D.	Philadelphia.

MÜTTER LECTURES

1865	J. H. Packard, M.D.	Philadelphia.
1866	J. H. Packard, M.D.	Philadelphia.
1867	J. H. Packard, M.D.	Philadelphia.
1868	Harrison Allen, M.D.	Philadelphia.
1869	J. H. Brinton, M.D.	Philadelphia.
1872	J. da S. Solis Cohen, M.D.	Philadelphia.
1879	S. W. Gross, M.D.	Philadelphia.
1882	E. O. Shakespeare, M.D.	Philadelphia.
1885	H. F. Formad, M.D.	Philadelphia.
1888	O. H. Allis, M.D.	Philadelphia.
1890–1891	Roswell Park, M.D.	Buffalo.
1893–1894	De Forrest Willard, M.D., and	Philadelphia.
	Guy Hinsdale, M.D.	Philadelphia.
1896	O. H. Allis, M.D.	Philadelphia.
1899–1900	J. B. Roberts, M.D.	Philadelphia.
1901	H. W. Cushing, M.D.	Boston.
1902	L. A. La Garde, M.D.	Washington.
1903	C. N. B. Camac, M.D.	New York.
1904	G. H. Monks, M.D.	Boston.
1905	A. O. J. Kelly, M.D.	Philadelphia.
1906	W. J. Mayo, M.D.	Rochester, Minn.
1907	J. Rogers, M.D., and	
	S. P. Beebe, M.D.	New York.
1908	G. W. Crile, M.D.	Cleveland.
1909	H. D. Fry, M.D.	Washington.
1910	T. W. Hastings, M.D.	New York.
1911	C. F. Nassau, M.D.	Philadelphia.
1912	J. C. Bloodgood, M.D.	Baltimore.
1913	R. C. Coffey, M.D.	Portland, Ore.
1914	F. H. Albee, M.D.	New York.

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